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SURGICAL TREATMENT IN TUBERCULOSIS COMPLICATED WITH PULMONARY EMPHYSEMA

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INTRODUCTION

THE surgical patient with generalized pulmonary emphysema presents a challenging problem in therapeutic management regardless of the nature of the proposed surgical procedure. In the patient with tuberculosis, complicated by the presence of generalized pulmonary emphysema, the need for objective thinking before electing to proceed with a needed surgical procedure is self-evident.[1, 2] This need stems from the current concept that, following long-term drug therapy and other methods of medical management, residual large foci of tuberculosis, whether air-bearing cavities or inspissated cavities or destroyed segments, lobes, or lungs, should be surgically treated; and in most quarters surgical treatment has meant surgical excision.[3-7] Thus, certain patients with tuberculosis, complicated with pulmonary emphysema, become candidates for major excisional or surgical collapse measures in the face of a deranged ventilatory and perfusion system.

We have followed the concept that, following adequate and for the most part prolonged (six to twenty-four months) medical management, the foci which the treatment had not been able to bring successfully under control due to mechanical problems[8] (i.e., bronchostenosis, bronchiectasis, residual cavities either air-bearing or solid) should be treated surgically. Following the lead of pioneers in the field, we became convinced early that resectional surgery offered better opportunities for correcting the surgical pathology and at the same time conserving pulmonary function at the highest possible level. Thus, inevitably, we began to accept patients for excisional therapy who had moderate to marked impairment of the pulmonary function prior to surgery due to pulmonary emphysema, regardless of the etiology. It followed that the problems concerned with management of these cases, during the operative and postoperative periods,

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soon became acutely real. Furthermore, it is anticipated that the number of patients with tuberculosis, complicated with emphysema, will increase as the trend in hospital admissions throughout the country is toward the older group of patients in whom the incidence of generalized emphysema is much higher. It is in this complicated group of older individuals that surgical therapy is usually mandatory if sputum conversion and arrest of the tuberculosis are to be accomplished.

Our presentation is an analysis of 30 surgical patients with tuberculosis complicated with moderate to far-advanced stages of pulmonary emphysema compared to a parallel group of 259 surgical patients treated during the same three-year period who had pulmonary tuberculosis without a significant degree of complicating emphysema. The complications and morbidity in the emphysematous group have been most impressive and prompted the undertaking of the study. This group also pointed to the need for a critical evaluation of the emphysematous patient prior to surgery and a keener appreciation of postoperative management directed toward the basic physiologic and pathologic deviations.

PATHOLOGY AND PATHOGENESIS

A. The basic tuberculous process takes place in the alveolar spaces, best seen in the acinous nodose foci developing beyond the terminal bronchiole.[9] Healing occurs by invasion of the fibrinocellular exudate in the alveoli by fibroblast, epithelioid, Langhans' cells, and collagen fibers. These elements replace the exudate; the collagen increases and an area of fibrosis develops which is surrounded by torn and stretched alveolar septa. As the granulation tissue is gradually replaced by connective tissue there is a gradual contraction of the focus. As the scar contracts it stretches the surrounding alveolar septa leading to perifocal emphysema.

Emphysema in pulmonary tuberculosis is a concomitant part of the destruction and resultant contraction of the lung parenchyma. As the tuberculous process progresses with necrosis and surrounding fibrosis, a compensatory dilatation of the surrounding air sacs develops. Since the parenchyma is a contiguous elastic structure, any replacement of it must be compensated for by a surrounding intact portion. This is done by stretching of the elastic fibers.

After chemotherapy, there is an over-all decrease in the amount of fibrosis and emphysema in patients who have received chemotherapy over a long period of time.[10] This is true if the drugs are given soon after the onset of the illness. The decrease is due to the elimination of the perifocal reaction resulting in decreased fibrosis and to the resultant decrease in dissemination. As a result of the greatly lessened fibrosis and emphysema in prolonged chemotherapy there is a greater normal lung volume. Intact lung parenchyma, which rarely contains scars, widely separates necrotic foci.

The bronchus communicating with a cavity almost always reveals the same ulcerative tuberculous process as that in the cavity.[9] The bronchocavity junction is a tangential canal resulting in a check-valve mechanism at this site. More air enters the cavity during inspiration than leaves during expiration, usually accounting for the spherical appearance.

Streptomycin treatment causes re-epithelization of the bronchus at the bronchocavity junction with extension along the inner wall of the cavity. This disrupts the check-valve mechanism allowing cavity healing to occur with the end result of an inspissated cavity with a patent communicating bronchus. "Open" healing is observed with increasing frequency after long-term chemotherapy, probably due to re-epithelization of the bronchus.

As a result of prolonged chemotherapy in pulmonary tuberculosis soon after its origin, the disease undergoes extensive resolution and the process is limited to a portion of a lobe or lung. The portion of residual diseased lung can then be removed surgically.

B. Obstructive emphysema in pulmonary tissue may be localized in a segment or lobe or it may be generalized throughout both lungs. It is brought about by an increased tension of the air within alveoli due to a partial occlusion of a bronchus or to a generalized increased air tension due to a partial occlusion of the respiratory bronchioles. The mechanism of the production by air-trapping in the alveolus by obstruction to the outflow of air is well known.[11]

The anatomy of the bronchial musculature indicates smooth muscle and elastic fiber projections to form sphincters about the atrial openings from the respiratory bronchioles.[12] Thus, trapping of air in the alveoli could result from sphincteric closure with outflow obstruction. Cough derived from any cause forces air into the alveoli under pressure which in generalized bronchospastic states or in localized segmental or lobular bronchitis produces an outflow obstruction. If this situation continues it will lead to alveolar overdistention, loss of elasticity in the bronchiolar walls, and permanent changes recognized as pulmonary emphysema. The emphysema may be localized or generalized.

Collateral air-drift as a safety device to prevent overdistention in a lobule or segment remains operative in most instances. However, in some cases it fails to keep the lobule deflated and bullae develop.[13] The process of obstructive emphysema is reversible unless it is prolonged and damage occurs to the elastic tissue in the alveoli; then the emphysema is permanent as the elastic tissue fails to recoil after stretching. In addition, alveolar septa become destroyed, leading finally to a gross cystic structure attached to one or several bronchi or bronchioles. The pulmonary vessels to the cystic area are obliterated. If diffuse emphysema is present in both lungs, peripheral resistance to the outflow tract from the right heart is increased and may lead to cor pulmonale. We have been impressed in our emphysema surgical cases with the markedly increased bronchial artery and bronchial vein blood flow; collateral circulation in both these systemic channels has been noticeable. Liebow and co-workers[14, 15] have written brilliantly on these collaterals and have further described sizable anastomoses between the bronchial and pulmonary arterial systems which represent points of peripheral resistance within the lung and, when sufficiently numerous, increase the work of the right ventricle. In addition, sizable shunts between the bronchial and pulmonary veins exist in emphysema. The exact mechanism is not known. One proposed mechanism would be due, according to the opinion of Loeschcke quoted by Liebow, to the fact that the bullae of

emphysema represent expanded portions of the lung tree more proximal than alveoli and include respiratory bronchioles. Then, the venous drainage of the cystic structures, as well as the arterial supply, is systemic in nature rather than from the lesser circulation. Another factor favoring augmentation of the bronchial arterial and venule blood flow is the loss of blood-pumping action from the alternating respiratory pressure changes as they affect the small vessels of a normally elastic parenchyma. This will tend to abolish the differential negative pressure, occurring with each inspiration, which ordinarily favors the flow of blood into pulmonary venules rather than bronchial venules.

The frequent anatomic location of bullae (or "cysts") in the apical segment of the upper lobe and in the superior segment of the lower lobe coincides with the frequent lobar apical localization of tuberculous cavities, which fact leads to interesting speculative possibilities as to the pathogenesis of tuberculous cavities; and further to their frequent failure to respond in emphysematous patients to conservative medical management by cavity closure.

In emphysema, the loss of lung elasticity greatly alters the efficiency of ventilatory function. Respiratory efficiency is decreased because of: (1) The overstretched inelastic subpleural alveoli cannot transmit the pull of the chest wall and diaphragm musculature to the underlying alveoli deeper toward the hilum. This leads to an increase in volume at the tidal expiratory level. (2) Increased ventilatory effort is required to maintain exchange in large lung volume. (3) The diaphragm is depressed in the larger lung volume. (4) The tidal air is unfavorably diluted by the increased residual volume.

Thus, in an emphysematous patient, the residual air may be as large as 50 to 60 per cent of the total lung volume, which leads to dilution of the tidal air.[16] The element of bronchospasm further reduces an already lowered maximum breathing capacity. Carbon dioxide retention is increased and oxygen tension at the alveolocapillary membrane is reduced.

CASE DATA

Our clinical material consists of 289 cases treated surgically for pulmonary tuberculosis. The cases are divided into 2 groups, the first group of 30 cases of tuberculosis, complicated with moderate to far-advanced pulmonary emphysema, and the second group of 259 cases of tuberculosis without a significant clinical degree of pulmonary emphysema.

The patients with clinical pulmonary emphysema are divided into a group with predominant obstructive emphysema and a group with predominant compensatory emphysema. The nonemphysematous group failed to show a significant degree of clinical emphysema changes although, undoubtedly in most cases of moderate and far-advanced tuberculosis, compensatory overdistention occurred as healing progressed. In the 30 emphysematous patients, 26 showed a predominant obstructive complex and 4 showed a predominant compensatory complex of marked degree.

The diagnosis of emphysema was established by: (1) History of "asthma" or asthmatoid wheezing. (2) X-ray evidence of increased radiolucency; depressed and flattened diaphragms; increased anterior-posterior diameter of

chest. (3) Fluoroscopic evidence of limitation of diaphragmatic excursion and failure of the lung alternately to lighten and darken with the respiratory cycle. (4) Bronchoscopic examination evidence of a nonspecific bronchitis and bronchospasm. (5) Bronchography was used to outline areas of compensatory emphysema. The distribution of the medium is striking in obstructive emphysema. (6) Ventilatory function studies were used in evaluation and diagnosis. Percentage timed vital capacity is the most helpful in making the diagnosis of the person with obstructive emphysema. The maximum breathing capacity is used in evaluation of the patient's ability to tolerate the surgical procedure. (7) An electrocardiogram which revealed right axis deviation. (8) The operative findings at the time of thoracotomy and pathologic examination of resected specimens were used to confirm the preoperative clinical impression.

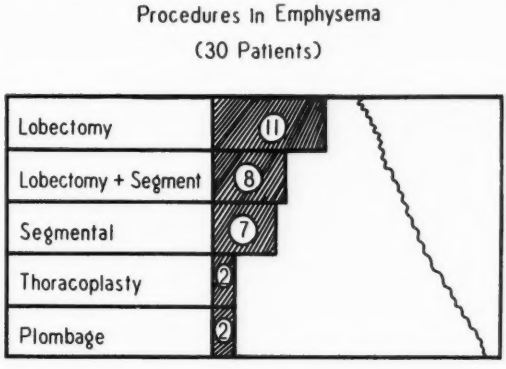

Fig. 1.

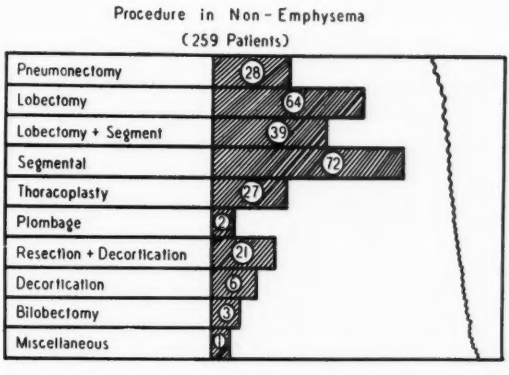

Fig. 2.

The patients were all treated medically with supervised bed rest and long-term antimicrobial therapy. Selected patients were treated with temporary collapse measures such as pneumoperitoneum and, occasionally, with pneumothorax. The preoperative treatment period ranged from six to twenty-four months. Postoperative treatment was continued in most instances from six

to twelve months. Postoperative follow-up has been most satisfactory in 96.2 per cent of the cases. Of the emphysematous group, 26.6 per cent had a positive sputum prior to surgery whereas 22.4 per cent of the nonemphysematous group failed to convert to negative sputum before surgery.

The operative procedure employed in the 2 groups of patients are shown in Figs. 1 and 2.

The complications in the 2 groups are shown in Table I.

TABLE I. COMPLICATIONS IN BOTH GROUPS

WITH EMPHYSEMA (%)	COMPLICATION	WITHOUT EMPHYSEMA (%)
57.6	BPF*—delayed re-expansion, no empyema	6.1
19.2	BPF—empyema	3.9
0.0	Empyema—no fistula	1.7
6.6	Spread	3.4
23.3	Miscellaneous	5.0
10.0	Cor pulmonale	0.0
19.2	Residual space	19.6
34.6	Secondary surgery	15.0
23.3	Status—active (31)	11.9†
6.6	(2) Deaths (8)	3.1

*Bronchopleural fistula.
†Included as active are 10 cases less than six months postoperative.

TABLE II. DEATHS IN GROUP WITH EMPHYSEMA

CASE NUMBER	AGE	VENTILATORY FUNCTION	PROCEDURE	CAUSE OF DEATH
415	WM-45	(%) 55—1 sec. 60—2 sec. 97—3 sec. *VC-4,000 L. †MBC-71 L./min.	Preliminary TP‡ stage RUL and Superior Segment RLL	BPF—empyema; death 6 weeks postoperative; hemorrhage; intrapleural
824	WM-43	(%) 56—1 sec. 65—2 sec. 81—3 sec. VC-3,200 L. MBC-63 L./min.	Preliminary TP stage RUL and Superior Segment RLL	BPF—empyema; cor pulmonale; pulmonary insufficiency; death 6 months postoperative

*VC = vital capacity.
†MBC = maximum breathing capacity.
‡TP = thoracoplasty.

The complications in the group of 30 cases of emphysema were numerous and in some instances multiple. In 8 cases, there were no complications and in this group were 4 patients having extrapleural operations. Twenty-two patients out of 26 cases of resection had thirty-seven serious complications with two deaths, a mortality rate of 6.6 per cent. Nine patients required major secondary surgery to correct the complications and 4 required prolonged chest drainage before eventually recovering. In the surviving group, 7 patients are alive but with active disease or with serious residual complications.

On the other hand, the surgical results in the group of 259 cases without serious emphysema have been most satisfactory. Bronchopleural fistula with

TABLE III. DEATHS IN GROUP WITHOUT EMPHYSEMA

CASE NUMBER	AGE	VENTILATORY FUNCTION	PROCEDURE	CAUSE OF DEATH
131	CF-40	VC-1,000 L.	Pneumonectomy	Cardiac failure, 6 months postoperative
151	WF-35	VC-1,000 L.	Pneumonectomy	Pulmonary insufficiency and cardiac failure, 2 weeks postoperative
271	WF-38	VC-1,400 L.	Pneumonectomy	Pulmonary insufficiency and cardiac failure, 8 days postoperative
510	WF-35	VC-1,300 L. (%) 46—1 sec. 69—2 sec. 84—3 sec. MBC-24 L./min.	Monaldi, 1 year; thoracoplasty I; pneumonectomy	Pulmonary insufficiency, 2 days postoperative
213	WF-40	No studies	RUL	Anesthesia death; cardiac arrest at conclusion of procedure
961	WF-32	VC-1,450 L. (%) 62—1 sec. 82—2 sec. 89—3 sec. MBC-27 L./min.	RUL and segment	Air embolism during transfusion, 3 days postoperative
93	CM-28	VC-1,900 L.	Thoracoplasty	Shock during surgery
356	WM-41	VC-1,900 L. (%) 73—1 sec. 82—2 sec. 100—3 sec. MBC-38 L./min.	Decortication	Died 3 days postoperative; pulmonary insufficiency, intrapleural hemorrhage, shock

empyema was present in 3.9 per cent and bronchopleural fistula without empyema (air-leak over seven days and with delayed re-expansion) in 6.1 per cent. Secondary surgery was performed in 15 per cent. The mortality rate was 3.1 per cent. These patients, now well and classified inactive, number 228 or 88 per cent. (Included as active are 10 cases yet in the hospital having been operated upon less than six months ago.)

EVALUATION OF THE PATIENT WITH EMPHYSEMA AND AN ESTIMATION OF HIS ABILITY TO TOLERATE SURGERY

Modern surgical philosophy[17] in the treatment of tuberculosis dictates not only a correction of the inflammatory process but the preservation of pulmonary function at the highest possible level. The mortality rate for resection and surgical collapse is now so favorable that a good result is no longer gauged by inactivation of the tuberculous process; in addition, cardiopulmonary reserves should not be compromised. If severe postoperative complications are encountered, these criteria will not be fulfilled.

Diffuse airway obstruction, as is commonly found in obstructive emphysema and in severe compensatory emphysema, is the chief cause of operative and postoperative difficulty. The complications which occur in this situation seriously impair the cardiopulmonary reserves. It is important that obstructive and compensatory emphysema of a moderate or severe degree be recognized prior to surgery and a surgical procedure selected and operatively managed to assure arrest of the tuberculosis and, also, preservation of respiratory function.

Evaluation of the surgical candidate is based on clinical study and certain simple ventilatory function tests in all cases. In selected individuals, special tests are performed. Clinical study includes the usual history and physical examination. Careful attention is paid to a history of wheezing or of "asthmatic attacks," as well as x-ray evidence of a depressed and deformed diaphragm, of increased radiolucency of the lung fields, of widening of the intercostal spaces, and of increased anterior-posterior diameter of the chest on the lateral x-ray projection. Fluoroscopic observation is done with particular attention to the degree of filling and emptying of the lungs, diaphragmatic movements, regional or diffuse airway obstruction, abnormalities of the cardiac shadow, and any abnormalities in cardiac action.

A simple ventilatory test found to be useful in our hands is the maximum breathing capacity which measures the ability of the patient to pump air in and out of the lungs. Several factors enter into the patient's ability to perform this test; first, the neuromuscular function of the chest wall and diaphragm; second, the ability of the lung to distend and collapse; and third, the patency of the airway. Impairment of any of these factors leads to a lowering of the maximum breathing capacity. The other most important over-all function test, especially significant in obstructive emphysema, is the percentage timed vital capacity three-second test. In our hands, it has been most reliable in distinguishing the patient with a high vital capacity and a good maximum breathing capacity who has a large residual volume due to obstructive emphysema.

TABLE IV. EVALUATION OF PATIENTS FOR SURGERY; FUNCTION STUDIES

1. Vital capacity; calculation of per cent predicted
2. Maximum breathing capacity; calculation of predicted
3. Timed vital capacity; per cent exhaled during 1, 2, 3 seconds
4. Walking ventilation
5. Calculation of walking index. WI = 100 × WV/MBC
6. Fluoroscopic examination
7. Bronchoscopic examination
8. Bronchography
9. Bronchospirometry (selected cases) differential (per cent O_2 uptake, ventilation, and VC)
10. Electrocardiogram

Evidence of carbon dioxide retention is important but it can be assumed that the person with diffuse obstructive emphysema is either retaining CO_2 or is unable to rid his blood normally of CO_2 due to the dilution factor at the alveolocapillary membrane. We have not done gas analyses on our patients.

Bronchoscopy is used in all our cases preparatory to treatment and also for surgical evaluation. Evidence of diffuse or regional bronchitis, severe bronchospasm, or bronchostenosis are all recognized and assist in surgical and treatment decisions. Bronchography is most useful in evaluation and diagnosis of the compensatory or obstructive emphysema patient. It is used primarily to outline areas of bronchiectasis or bronchostenosis.

Bronchospirometry is reserved for patients with altered function in whom it is desirable to know to what extent each lung participates in ventilation and gas exchange.

The knowledge of the degree which lungs resist distention and collapse as ascertained by the MBC (maximum breathing capacity) is important when considering an emphysema patient with a "flail chest" due to extensive decostalization procedures. Airway obstruction of emphysema causes the flaccid chest wall to move in further with each inspiration and move out further with each expiration.

Diffuse airway obstruction of pulmonary emphysema or severe compensatory emphysema interferes with proper ventilatory exchange in the alveoli and leads to hypoxia and also to CO_2 retention and respiratory acidosis. The development of respiratory acidosis and cardiac arrhythmias, during operation and in the postoperative period, is recognized and is especially prone to develop in patients with severe ventilatory derangement.[18]

THE "EMPHYSEMA SYNDROME"—A POSTOPERATIVE PROBLEM

The surgical patient with pulmonary emphysema presents a striking, characteristic clinical picture in the postoperative period. The condition is best described as the "emphysema syndrome," as it is a physiologic and pathologic alteration brought on by profound changes in the body mechanism.

Dehydration is a prominent sign and is manifested by poor tissue turgor, dry skin, dry, beefy-red tongue, and oliguria. It is present despite what appears to be an adequate water intake. It is related chiefly to an increased insensible loss of water through the respiratory system related to the hyperventilation of emphysema. Dehydration is prominently associated with respiratory acidosis.

TABLE V. "EMPHYSEMA SYNDROME"

1. Dehydration
2. Hyperventilation
3. Respiratory acidosis; alteration in blood CO_2, sodium, and potassium
4. Toxicity due to retained bronchial secretions
5. Marked paradoxical movement in thoracoplasty cases
6. Protracted air leak in resection cases
7. Intestinal distention
8. Disorientation and hallucinations

Hyperventilation is the only physiologic method that the severe emphysematous patient has to compensate for his inadequate alveolar ventilation and perfusion. Chronic arterial anoxia and carbon dioxide must be combatted and an increased depth and rate of respiration is his only recourse.

Respiratory acidosis may be present in this symptom complex. Hyperpnea and dyspnea with mild exertion are the only fairly constant signs associated with a nondiabetic acidosis.[19] However, when the acidosis is severe breathing may be normal even though the plasma pH is very acid. Tachycardia and headache are inconstant signs. Respiratory acidosis may be present and the only sign be a dyspnea out of proportion to the work being performed. Very severe respiratory acidosis is attended by signs of dying such as weakness, disorientation, stupor, and coma. The CO_2 combining power of the plasma may be elevated as a compensatory reaction to a long-standing CO_2 acidosis as measured preoperatively and be not at all indicative of an alkalosis. Potassium

deficits tend to complicate severe extracellular fluid volume deficiency. Alkalosis or acidosis accelerates the inception of potassium deficit for reasons not well understood.

Signs of toxicity with moderate fever, tachycardia, and leukocytosis are related to retained bronchial secretions and lobar or segmental atelectasis. The cleansing mechanism of the bronchus in emphysema is markedly interfered with by the elongation and fixation of the trachea and large bronchi. Ciliary action and bronchial peristalsis are inefficient. Cough of an effective nature depends on movable air and, in emphysema cough is ineffective due to the marked increase in residual air volume. In addition, acute atelectasis contributes markedly to the degree of arterial unsaturation due to venous admixing from the perfused but nonventilated lung.[20]

The marked paradoxical movement in thoracoplasty cases with the resultant poor air exchange is self-explanatory. Protracted air leak from the raw surface of the lung in segmental resections and from undeveloped or fused interlobar fissures has been a major problem. The continued air leak necessitates prolonged tube drainage with the increased likelihood of pleural contamination.

Intestinal distention of moderate to major proportions has been evident. One factor is probably due to swallowed air in the hyperventilating and anoxemic individuals, and a second is the intestinal distention that accompanies hypokalemia. A third factor is related to the abdominal type respiration which most of these emphysema patients depend upon, especially in those with fixed thoracic cages.

Disorientation and hallucinations are seen frequently and are prone to develop in the patient with respiratory acidosis of a moderate or severe degree—these are usually late signs and indicate marked metabolic derangements.

CLINICAL APPLICATION OF SOLUTION TO PROBLEM AS DERIVED FROM OUR EXPERIENCES

A. *Selection of Operative Procedure.*—Numerous previous discussions attest to the divergent opinions with regard to the surgical treatment of pulmonary emphysema per se and also as to the management of overdistention of the residual lung or lung tissues following pulmonary resection. It has been pointed out that a postoperative reactivation or spread of tuberculosis in the emphysematous lung causes the patient to do poorly and usually to an extent proportional to the degree of emphysema.[10] From our studies, we would conclude that the patient with tuberculosis and diffuse obstructive pulmonary emphysema does poorly with resectional surgery in a high percentage of cases. Resectional surgery in the patient with compensatory emphysema of even a marked degree is associated with fairly good results. An upper preliminary stage of thoracoplasty of two or three ribs prior to the resection helps to ensure eradication of any space problems and assists in overcoming persistent air leaks. If a bronchopleural fistula and empyema develop, the resultant space will be small. Sufficient interval should elapse between the stage of thoracoplasty and the resection so that a relatively stable chest wall will be present postresection, otherwise, paradoxical movement of the chest wall will negate the value of the preliminary thoracoplasty.

TABLE VI. SELECTION OF OPERATIVE PROCEDURE

1. Preresection thoracoplasty (small stages)
2. Monaldi tube—long-time suction followed by thoracoplasty
3. Extraperiosteal plombage
4. Primary resection—especially in cases of compensatory emphysema

The value of Monaldi catheter suction in obliterating large, tension tuberculous cavities is time-proved[21] and in the patient with associated obstructive emphysema it can be life saving. The long-term catheter suction treatment should be followed by an extrapleural thoracoplasty to ensure permanent collapse of the diseased area. Perhaps the idea of converting the sputum to negative will not be realized in all cases but more patients will be alive to have sputum.

Extraperiosteal plombage is an excellent alternative method in selected cases. The function-sparing aspects of this operation have been repeatedly shown. It is particularly useful in apical, bilateral, cavitary disease. The emphysematous patient tolerates the procedure well. The disadvantage of inserting a foreign material in the body is recognized, but with careful technique only a few will become complicated, and if so the prosthesis can be removed and a thoracoplasty added to obliterate the resultant space.

The combination of a lowered maximum breathing capacity and of a low percentage timed vital capacity in a patient with obstructive emphysema is a very poor prognostic sign and would serve to indicate that resectional surgery is contraindicated. Our results would indicate that these patients tolerate the operative procedure very well but the high percentage of postoperative complications, led by bronchopleural fistula, tend to cause postoperative derangement which is insurmountable. On the other hand, a patient with a good maximum breathing capacity but with a low percentage timed vital capacity will probably have difficulty but will survive, although the complications of resectional surgery will compromise function in the remaining lung tissue.

B. *Operative Management.*—Preoperative treatment should be directed toward relief of bronchospasm with bronchodilator drugs. Expectorant mixtures should be used. Postural drainage and the use of the intermittent positive pressure breathing apparatus with exhalator phase is recommended. Avoidance of cigarettes or cigars is advised. Adequate parenteral fluids and electrolytes should be given to improve the extracellular fluid compartment and to establish the blood CO_2, sodium, and potassium at normal levels. Digitalization in the cor pulmonale cases is indicated. It is desirable to have a negative sputum or at least have drug-sensitive bacilli at the time of operation.

The anesthetic management during surgery is a particularly important phase. It is important that respiration be assisted even to the point of hyperventilation throughout although it is difficult to avoid CO_2 accumulation and resultant acidosis during open-chest operations. Greatly prolonged operating time is to be avoided as there is a direct relationship between time elapsed and degree of CO_2 retention and resultant acidosis. Blood replacement therapy

should be exact by the dry-sponge weight calculation method. The choice of agent depends on the judgment in each case, although our choice in bronchospastic states has been a gas-ether-oxygen combination.

We feel that the use of tracheostomy at the time of surgery will do much toward solving some of the postoperative difficulty with the "emphysema syndrome."[22] By eliminating 100 to 150 c.c. of "dead air" space, effective movement of tidal air is facilitated. The dilution factor at the alveolar membrane is reduced and by having ready access to catheter suction of secretions airway cleansing is effective. Any paradoxical movement can be controlled and paradoxical motion is a big problem in obstructive emphysema. Tracheostomy requires constant supervision by trained personnel; effective cough mechanism is lost in intubated patients. If tracheostomy is not done, then frequent use of endotracheal suction or bronchoscopy is indicated to secure airway patency and to prevent atelectasis.

Careful attention to fluid and ion requirements, especially accounting for the insensible water loss due to hyperventilation is necessary.

The usual antimicrobial regime is utilized postoperatively, frequently combined with the broad spectrum antibiotics.

TABLE VII. POSTOPERATIVE MANAGEMENT OF "EMPHYSEMA SYNDROME"

1. Parenteral fluids
2. Correction of CO_2, sodium, and potassium imbalances
3. Tracheostomy (early in selected cases)
4. Bronchoscopy plus catheter suction
5. Bronchodilator drugs
6. Intermittent positive pressure breathing
7. Antibiotics
8. Avoidance of paradoxical motion
9. Sparing use of narcotics
10. Digitalization as indicated

In conclusion, we feel that there is no larger, unsolved problem in the thoracic surgical field than the patient with obstructive emphysema. The problems are manifold and his treatment is complicated. When the emphysema is complicated by tuberculosis (or the tuberculosis complicated by emphysema), he becomes a community problem and as such becomes eventually a candidate for surgical treatment. The major points to be considered in the surgical management are (1) the selection of an operative procedure designed to arrest the tuberculosis and conserve pulmonary function at a level compatible with an active but restricted life; (2) preoperative and operative management to correct, in so far as possible, the deranged ventilatory function which has altered the basic mechanism of the body; and (3) prompt recognition of postoperative complications and institution of corrective measures.

SUMMARY

1. The surgical treatment of pulmonary tuberculosis complicated with either severe obstructive or compensatory emphysema is marked by multiple complications in the postoperative period. The complications are particularly severe if resectional surgery is performed.

2. Comparative studies on results obtained in the surgical treatment of 30 patients with tuberculosis and pulmonary emphysema are made with 259 patients with relatively uncomplicated tuberculosis. The incidence of bronchopleural fistula with empyema, and persistent air leak without empyema was remarkably high in the emphysema group. Bronchopleural fistula with empyema was the complication resulting in the two deaths out of the 30 cases; a mortality rate of 6.6 per cent. In the nonemphysema group of 259 cases, eight deaths occurred, a rate of 3.1 per cent, none of which were due to bronchopleural fistula or empyema.

3. The "emphysema syndrome" is described and suggestions as to operative management are made.

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Discussion

DR. AUSTIN R. GRANT, Brooklyn, N. Y.—In resectional therapy of cases where the remaining lung tissue is emphysematous, a major consideration is to prevent abnormal volumetric changes of the remaining parenchyma. In order to prevent these changes, an intrapleural tailoring procedure, originally devised by Dr. Miscall and Dr. Klopstock in 1947, is now being used and studied by Dr. Klopstock, Dr. Seibens, and me at the Veterans Administration Hospital, Brooklyn, N. Y., in patients with emphysema of the lung and where large segments of lung have been excised.

The method consists of reroofing the pleural cavity with a sheet of parietal pleura following partial pulmonary resection. It is tailored to the configuration of the residual pulmonary parenchyma, thus eliminating any residual space.

It is accomplished without the trauma of rib resection. Importantly, it prevents sudden overdistention of the residual pulmonary parenchyma, allowing a subsequent graded and adaptable rate of pulmonary expansion. The tent minimizes respiratory distress in the patient with marginal pulmonary reserve. It is useful in bilateral procedures and is relatively reversible.

A patient, H. A., with bilateral cystic disease and emphysema had an excision of a left lung cyst with pleural tent on July 24, 1954, and a right upper lobectomy with a pleural tent on Nov. 10, 1954. The preoperative and postoperative roentgenograms are shown.

Postoperative pulmonary fuctional studies reveal a decrease in residual volume, a decrease in vital capacity, an unchanged ratio of residual value to total lung capacity, and an increased maximum breathing capacity. This is a desirable and favorable functional result, avoiding the abnormalities of volumetric relationships which occur in overdistention of lung parenchyma.

A color film shows the technique of reroofing with a pleural tent.

Postoperative roentgenograms of a second patient illustrate the immediate selective limitation of expansion of the residual lung and the subsequent gradual incomplete absorption of fluid and air above the tent.

DR. WILL C. SEALY, Durham, N. C.—Respiratory acidosis is a frequent and difficult problem in the management of emphysematous patients. It is one that we have to deal with not only during operation but in the immediate postoperative period as well.

(slide) This is not a patient with tuberculosis, but one with a spontaneous pneumothorax that has been present for six months, associated with a bronchopleural fistula. This patient had markedly impaired respiratory function.

(slide) This shows a preoperative determination of the carbon dioxide tension of the blood. He had marked ventilatory impairment with a pCO_2 of 65 mm. Hg, and an oxygen saturation of 82 per cent. He had a left thoracotomy with decortication and expansion of the left lung. He did quite well during the procedure, but on the first postoperative day the systolic blood pressure was found to be below 100. He was semicomatose. At that time the pCO_2 had increased to 169 mm. Hg, the pH had dropped to 6.97, and the oxygen saturation increased to 99 per cent. The nasal oxygen administration was stopped. In twelve minutes' time, the pCO_2 dropped to 119 and the oxygen saturation to 89 per cent. This patient made an uneventful recovery, the mental changes cleared completely, and at the time of his discharge the oxygen saturation was back to 95 per cent, and there was only a slight elevation in pCO_2. Patients with chronic respiratory acidosis breathe by means of the hypoxic stimulus to the aortic and carotid bodies; and if this stimulus is removed, they go into marked ventilatory suppression, causing the CO_2 to increase further, followed by coma.

(slide) This shows a preoperative film on a patient with carcinoma of the lung, whose condition was quite good before operation. The next slide shows what happened following surgery.

(slide) The second day after operation he developed expiratory wheezes with bronchial obstruction. On the seventh day he became semicomatose. He was started on ACTH, and in the meantime had frequent aspirations by bronchoscopy. On the ninth day we found the pCO_2 had increased from 67 to 96 mm. Hg. The pH had dropped from 7.38 to 7.16. He was completely comatose. We then did a tracheotomy, put him in a Drinker respirator, and gave him intravenous cortisone. He gradually improved. On the tenth day we removed him from the respirator, and he made an uneventful recovery. At the time he left the hospital he still had chronic respiratory acidosis because of emphysema.

Postoperative respiratory acidosis is a more widely prevalent problem than is generally recognized. It can be easily confused with cardiac failure and cerebral embolus. One should be aware of this possibility when oxygen is administered to postoperative emphysematous patients. Its presence can be proved by estimation of pCO_2 and pH on arterial blood.

DR. NEWMAN, (Closing).—I should like to thank the discussants, and to say a word or two more about operative management. We think that the management of these patients during the operative period is particularly important; it is important that respiration be assisted even to the point of hyperventilation, and at the conclusion of the operation, when the patient has been recognized as being one who is going to have difficulty from what we call the "emphysematous syndrome" postoperatively, we do a tracheotomy at the time, before the patient leaves the table. This, we think, does much toward solving the majority of the postoperative problems, because by eliminating approximately 100 to 150 c.c. of "dead air" space, effective movement of the tidal air is facilitated and the dilution factor at the alveolar membrane is reduced.

In conclusion, then, we feel that there is no larger, unsolved problem in the thoracic surgical field than the patient with obstructive emphysema. The problem is manifold and the treatment is complicated. Emphysema complicated with tuberculosis becomes a community problem, and a patient with such a combination usually becomes a candidate for surgical treatment.

SURGERY FOR CAVITARY TUBERCULOSIS IN PATIENTS WITH A SINGLE LUNG

FRANCIS M. WOODS, M.D., NORMAN J. WILSON, M.D., AND
RICHARD H. OVERHOLT, M.D.
BOSTON, MASS.

THE management of a segment or lobe destroyed by tuberculosis in the lung remaining after a contralateral pneumonectomy presents a real challenge when it will not respond to antimicrobial treatment. Pneumothorax has been tried. We have attempted cavity drainage, Monaldi drainage, modified thoracoplasties, and extrapleural collapse, usually without favorable issue.

All these procedures significantly reduce the function of the uninvolved segments. Resection of diseased and useless segments or lobes decreases function to a lesser degree if the thoracic cage is opened and then repaired anatomically. The benefits of excisional therapy need not always be withheld from patients possessing only one lung.

In 1951, the successful wedge resection of an isolated metastasis in a single remaining lung was reported by Waterman. Shortly afterward we were asked to help a young pregnant mother with a ballooned-up cavity in the apical segment of the right lower lobe. The left lung had been resected. The diseased segment was surgically excised and she recovered and later delivered normally. The baby is well. The mother is alive, although restricted in her activity. This experience has led us to attempt to salvage 5 additional patients with tuberculous lesions in the lung remaining after a pneumonectomy (Table I). All had failed to respond to prolonged and varied antibacterial therapy.

The surprising feature of the operative procedure has been that in the face-down position the patients were carried through an uneventful anesthesia with respirations only lightly assisted. An endotracheal tube was inserted under topical cocaine. Cyclopropane induction was followed by ether-oxygen maintenance manually assisted when the chest was open. The thoracic cage was entered through an interspace with only one or two ribs divided posteriorly. In closing, the cut ribs were notched, interlocked, and sutured together and the interspace closed thus restoring chest wall contour and stability and motion.

The operative procedure was but slightly hampered by the constant slow rhythmic inflation and deflation of the lung. Only limited resections were undertaken. This involved one subsegmental, four segmental, and two lobar resections. At the close, two intrapleural catheters were used for underwater seal drainage with regulated suction. Postoperatively, particular attention was paid to management of bronchial secretions and maintenance of a good airway.

From the Overholt Thoracic Clinic, Boston, Mass.
Read at the Thirty-fifth Annual Meeting of The American Association for Thoracic Surgery at Atlantic City, N. J., April 24 to 26, 1955.

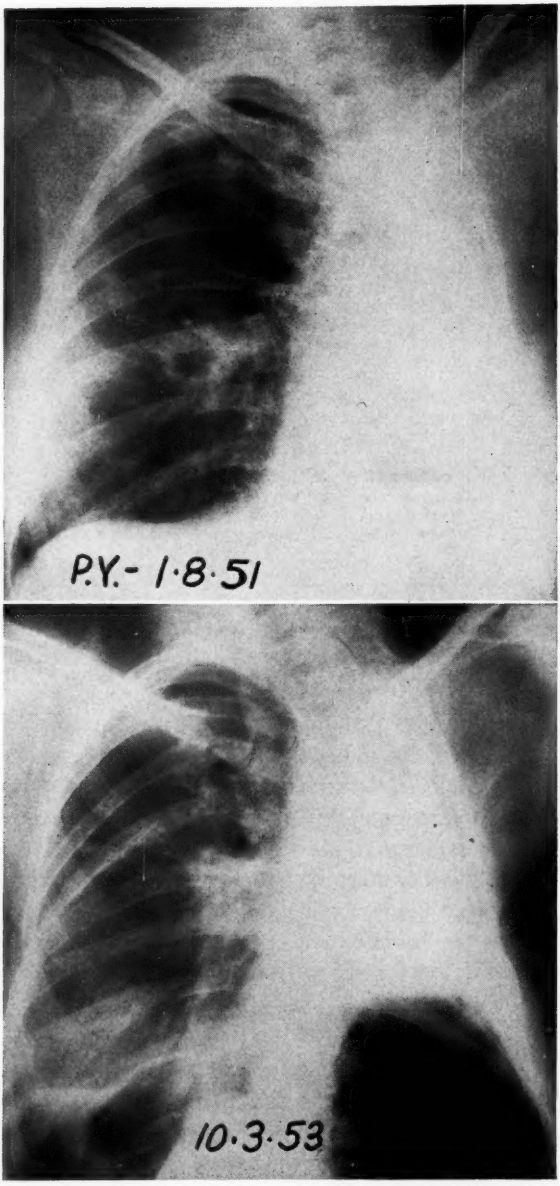
TABLE I. CASE SUMMARIES

NAME	AGE	SEX	PNEUMONECTOMY	RESECTION ON REMAINING LUNG	COMPLICATIONS	RESULT (APRIL, 1955)
1. P. Y.	32	F	Left, Mar. 30, 1948 Destroyed lung	Superior seg. right lower cavity tuberculosis, Jan. 19, 1951	4 mo. pregnancy, bronchoscopy 4th day Spontaneous pneumothorax, 7th day	Alive, sputum positive X-ray stable
2. J. G.	48	M	Left, Jan. 21, 1950 Destroyed lung	Post. seg. right upper fibrocaseous tuberculosis with cavity, Mar. 26, 1952	Air leak and atelectasis	Death, fourth postoperative day
3. D. T.	37	F	Left, June 15, 1949 Destroyed lung, bronchostenosis	Subseg. apex right lower lobe, 4 cm. inspissated cavity, Oct. 28, 1952	None	Normal life, sputum neg.
4. F. Z.	32	F	Left, April 4, 1951 Destroyed lung	Right upper lobe; fibrocaseous tuberculosis with cavity, Dec. 30, 1952	None	Normal life, sputum neg.
5. M. O'L.	41	F	Left, June 13, 1951 Destroyed lung, bronchostenosis	Right upper lobectomy; fibrocaseous tuberculosis with cavity, Nov. 12, 1953	None	Normal life, sputum neg.
6. G. C.	24	F	Right, June 30, 1950 Destroyed lung, endobronchial disease	Superior seg., left lower lobe, wedge anterior seg. left upper; fibrocaseous tuberculosis with cavity, Nov. 12, 1953	None	Normal life, sputum neg.

Several factors seem worthy of consideration in choosing postpneumonectomy patients who can survive a limited resection in the remaining lung. *First,* age: younger individuals will tolerate greater resections. This group averaged 36 years of age, ranging from 24 to 48 years. *Second,* residual disease in the lobes and segments to remain and support life: very little emphysema or nodulation will be tolerated in these segments. The only death occurred in a 48-year-old man who had some palpable nodules in all the segments left after resection of the posterior segment of the right upper lobe. *Third,* side: the right lung is larger and, therefore, has a larger factor of safety. Five of these six resections were from the remaining right lung. Evaluation of adequacy of pulmonary function was based on clinical examination, particularly the ability to perform ordinary activity without dyspnea.

Five of the six apparently hopeless derelicts are alive. Four of them lead normal active lives, have consistently negative sputum and stable chest x-rays, one and one-half to two and one-half years since operation. Their operative and postoperative courses were uneventful. One patient, the first of the six, leads a restricted life and has intermittently positive sputum, but stable chest x-rays three and one-half years later. The one death, already alluded to, was in a patient with nodules in all residual segments. There was difficulty in attaining complete re-expansion of the lung and management of secretions. He died on the fourth postoperative day. The only other complication was spon-

A.

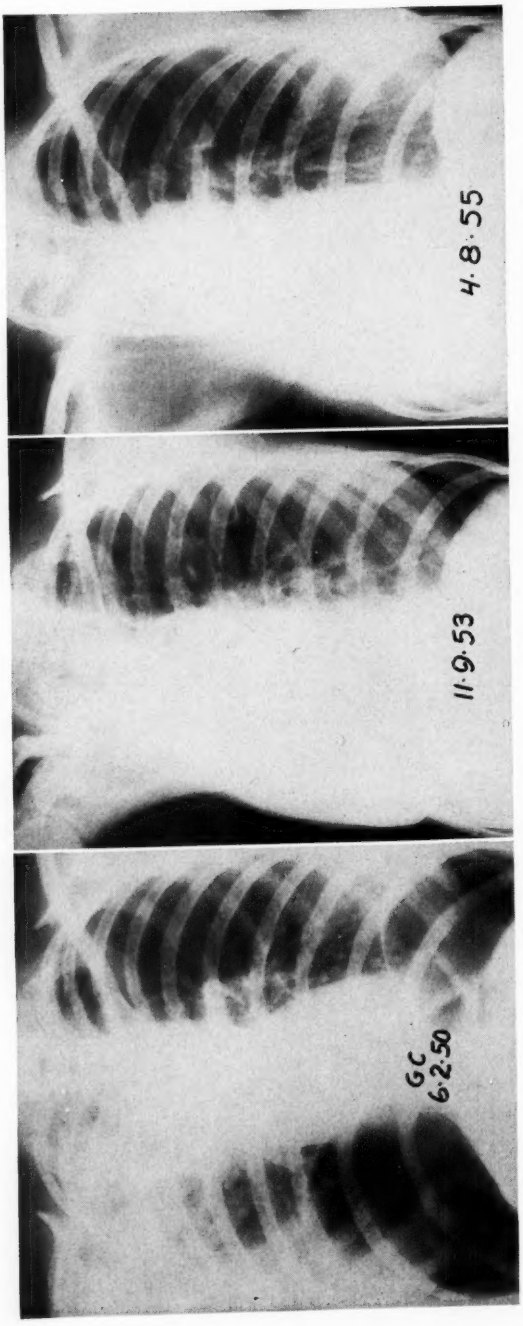


B.

Fig. 1.—*A* and *B*.

A. *B.* *C.*

Fig. 2.—*A*, *B*, and *C*.



A. B. C.

Fig. 3.—*A*, *B*, and *C*.

taneous pneumothorax occurring on the seventh postoperative day. Fortunately, an alert resident recognized the problem and promptly inserted an intrapleural catheter for underwater seal drainage.

CASE REPORTS

CASE 1. (P. Y.) The patient was a 32-year-old woman who had been treated for 11 years by left pneumothorax, thoracoplasty, and, finally, resection of a destroyed left lung in 1948. She had had several courses of streptomycin. After the pneumonectomy, she had intermittent positive sputum and an infiltrate in the right mid-lung field. On referral to us, she was four months pregnant and there was a cavity in the apex of the right lower lobe (Fig. 1, *A*). A segmental resection of this segment was carried out uneventfully on Jan. 9, 1951. She needed bronchoscopic aspiration on the fourth postoperative day and an intrapleural catheter inserted on the seventh postoperative day for tension pneumothorax. Despite continued and varied antibacterial drugs and pneumoperitoneum, she still has intermittently positive sputum. Her activity is limited to a quiet home life and the chest x-ray remains stable (Fig. 1, *B*).

CASE 4. (F. Z.) The patient was a 32-year-old woman who had been treated primarily for basal left-sided pulmonary tuberculosis since May, 1949, by rest and left phrenic nerve paralysis. In 1950, there was a right-sided spread with pregnancy. Later, treatment by pneumoperitoneum was added but left pneumonectomy and subsegment thoracoplasty were necessary in April, 1951. The right-sided lesion had cleared (Fig. 2, *A*), but later broke down and failed to respond to a series of antibacterial agents. Cavitation persisted. She was clinically well and x-ray study appeared to show all the disease in the apical and posterior segments of the right upper lobe (Fig. 2, *B*). On exploration of the right chest, the entire right upper lobe was found to be involved. It was removed and an uneventful convalescence ensued. She is home, well, active, and only slightly dyspneic on exertion. Chest x-ray remains clear (Fig. 2, *C*) and sputum negative.

CASE 6. (G. C.) The patient was a 24-year-old woman who had been treated for extensive parenchymal and endobronchial tuberculosis of the right lung beginning in May, 1949, with streptomycin, para-aminosalicylic acid, and pneumoperitoneum (Fig. 3, *A*). She had had a right pneumonectomy in June, 1950, and later a thoracoplasty. In January, 1951, there was a left-sided spread. By November, 1953, she was clinically well but had a persistent cavity in the apex of the left lower lobe (Fig. 3, *B*). A segmental resection of this segment was done together with a wedge from the anterior segment of the left upper lobe. No complications occurred and she is well with stable x-ray and negative sputum (April, 1955). (Fig. 3, *C*.)

SUMMARY

Fibrocaseous tuberculosis with cavity existing in the remaining lung after contralateral pneumonectomy which is resistant to antibacterial agents has presented an ordinarily insuperable therapeutic problem. Limited excision is possible, if the remaining segments are healthy. Younger patients will tolerate such excision best, particularly if the remaining lung is on the right. Six such resections have been carried out with 4 unqualified successes, 1 death, and 1 patient alive but with intermittently positive sputum.

Note: We have recently (Feb. 3, 1955) extended this procedure to a 63-year-old white man who had a segmental resection of the apical posterior and anterior segments of the left upper lobe for epidermoid carcinoma. He had had a right pneumonectomy for adenocarcinoma in August, 1950.

DISCUSSION

DR. E. E. ROCKEY, New York, N. Y.—I rise to present the case of a 53-year-old white man who was submitted to segmental resection of the remaining lung on June 1, 1950. He had undergone a left pneumonectomy in February, 1949, for undifferentiated carcinoma.

(Slide) Fifteen months later a recurrence of the disease was noted, which was located in the superior segment of the right lower lobe. The patient was submitted to a resection of the superior segment of this right lower lobe. He made an uneventful recovery and was discharged from the hospital twelve days following the operation. Within six weeks he returned to his usual occupation as a house painter. He remained well for an additional four months.

(Slide) An x-ray taken eight months following the segmental resection showed evidence of recurrence of the disease, and ten months following the segmental resection, a total of twenty-five months from the time of the left pneumonectomy, he died of generalized metastases.

DR. BERT H. COTTON, Los Angeles, Calif.—I rise for three reasons; first, to tell Drs. Francis Woods and Norman Wilson how much I have enjoyed their paper. Characteristic of their attitude and that of Dr. Overholt concerning resection for tuberculosis, they have surmounted technical difficulties to give the patients the best chance for cure. Second, since there seems to be a paucity of pulmonary resection in patients with a single lung, I should like to report 2 successful cases.

(Slide) This is an important decision to make in cases that are otherwise hopeless. However, I have viewed these cases with misgiving since our last case, which presented such a crucial and possibly criticizable decision.

The third reason is to show slides of this desperate case.

(Slide) The patient, a 45-year-old man, had coexisting tuberculosis and coccidioidomycosis with a destroyed left lung and empyema. A left extrapleural pneumonectomy was successfully performed but the patient continued to have hemoptysis with enlargement of the contralateral cavity. A right upper lobectomy, plus resection of the superior segment of the right lower lobe, was necessary to remove the multiple cavitation. The postoperative course was difficult due to fluid accumulation. The patient survived and did well.

DR. DAVID H. WATERMAN, Knoxville, Tenn.—The equanimity with which the papers this morning have been received testifies to the progress of thoracic surgery in the field of tuberculosis, and probably also testifies to the mellowing process that has taken place in many of the more articulate members of this Association. Certainly nothing is sacred. Dr. Woods and Dr. Wilson deserve particular commendation for their contribution.

Encouraged by our success in the case to which Dr. Woods referred, reported before this group in 1949, we have never hesitated to recommend surgical attack on the contralateral lung in pneumonectomized patients when we thought it was indicated. Certainly anesthesia is a very important point as Dr. Woods has mentioned; such surgery cannot be done without very competent and successfully controlled anesthesia. I might say, too, that it is important to cut down the operative time as much as possible, although I doubt if we can perform these operations quite as quickly as Dr. Grant did in his movie. Postoperative care is naturally of exceeding importance, as is the cooperation of the patient. Sometimes I am inclined to think that the patients we see at the State Tuberculosis Hospital and at some of our other sanitoriums are not quite as intelligent as those Dr. John Lewis sees at the State Mental Hospital.

I thought the Association might be interested in a brief follow-up on the patient on whom we reported at the meeting in 1949. This was a 52-year-old man who had had a left pneumonectomy performed in the fall of 1942 for a squamous-cell carcinoma of the left lower lobe. Six years later, in the fall of 1948, we resected an isolated metastasis in the posterior segment of the right upper lobe. His postoperative course was uneventful and he survived for more than two years, during which time he led an active business life. He died eventually of extensive liver metastases.

DR. JAMES E. DAILEY, Houston, Tex.—Despite the apparent ease with which Dr. Waterman shrugs off operating on pneumonectomized patients, it is certain that one thinks with some degree of hesitation about operating on a person with only one lung. Dr. Woods should be congratulated indeed on the nice series of cases that he has presented.

(Slide) I would like to show a case illustrating the number of insults some individuals with only one lung can put up with and still survive. This man, in May, 1950, had a large

squamous-cell carcinoma of the right lung. A little over a year after removing it, I was much surprised to see the right chest cavity filled with a large cyst containing air. This turned out to be a huge emphysematous bulla that crept across the anterior mediastinum from the left upper lobe and completely filled the right thoracic cavity. It caused no symptoms and the individual went along for a number of years with no trouble whatsoever until December, 1953, over a year ago.

(Slide) Suddenly, he developed a spontaneous tension pneumothorax and collapse of the left and only lung. Fortunately, I saw him quickly enough to put a tube in his chest, re-expanded the lung with suction and instilled 10 per cent glucose in the pleural cavity, hoping that pleural symphysis would occur. The lung re-expanded, he went home, and about a week later the same thing happened a second time. Again a tube was placed in the chest and the lung re-expanded. This time I placed 20 per cent glucose in the pleural cavity. He was again discharged to his home and three weeks later the lung collapsed for a third time. He was brought back to the hospital cyanotic and gasping for breath and a thoracotomy tube was reinserted. This time, since there was no LePage's glue handy, I inserted 50 per cent glucose. The lung re-expanded and I began to think of something to do to prevent any more such occurrences.

Finally, we got courage enough to operate. I opened the right chest, removed the tremendous bulla which completely filled the hemithorax, ligating and dividing it from the left upper lobe. I then filled the space with an Ivalon sponge prosthesis. That was in March, 1954. A little more than a year has now passed and the patient has been perfectly well to this date. Incidentally, he is a good example of a five-year cancer cure.

DR. RICHARD H. OVERHOLT, Boston, Mass.—I should like to report one case that is related to the technical problem of those presented by Dr. Woods. This case is rather unique in that it represents, I think, the only instance in which I sat by for several weeks in the presence of x-ray evidence of cancer and watched a shadow grow.

The patient was a 63-year-old doctor who had been treated for a carcinoma of the right lung by pneumonectomy four and one-half years previously. In May of last year, an area of density was noted in the apex of the remaining left lung. No investigation or treatment was advised. I saw him again in November after he had experienced a pulmonary hemorrhage. The x-ray revealed considerable enlargement of the area of density. It now occupied the upper third of the left lung field. He came back in January and wanted to know if I would not at least investigate and consider resection. Upon bronchoscopy, the left hilar structures were mobile. All studies of secretions were negative. A cervical node dissection was done and those were negative. He then said he was going to commit suicide if we did not stop the bleeding. He had had three or four rather frightening hemorrhages. I was then persuaded, somewhat against my better judgment, to explore the left chest. This was done, and we found the mediastinal nodes to be negative. We resected the posteroapical and anterior segments which contained the mass. A fairly large lingula and lower lobe were all that remained. He had a smoother convalescence following this operation than that following the right pneumonectomy. He was discharged on the seventeenth postoperative day.

(Slide) There is a final interesting point about this case. He had an epidermoid carcinoma on the first side and an adenocarcinoma on the other. He had been a heavy cigarette smoker. We persuaded him to give up the habit four and one-half years before. Surgery saved him from the cigarette-type cancer, and he lived long enough to develop a non-smoker's type of cancer.

He experiences only slight dyspnea on exertion and is free of all pulmonary symptoms. Recently, there was a urinary shutdown which required a transurethral prostatic resection.

DR. JOSEPH GORDON, Albuquerque, N. M.—I believe in the relationship between the reactivation of tuberculosis and overdistention of the lung, as was indicated in the paper on pulmonary distention presented two years ago. I should like to suggest to those of you who are contemplating a pneumonectomy in tuberculosis, to consider carefully any residual lesions in the contralateral lung and do a preliminary excision on those before embarking upon a pneumonectomy on the opposite side.

THE SURGICAL TREATMENT OF PULMONARY HISTOPLASMOSIS WITH AN EVALUATION OF MRD-112 AS A POSSIBLE ADJUNCT

JOHN W. POLK, M.D.* (BY INVITATION), CHARLES A. BRASHER, M.D.** (BY INVITATION), JOAO DECASTRO, M.D.*** (BY INVITATION), AND W. W. BUCKINGHAM, M.D.****
MT. VERNON, MO.

DARLING in 1906 gave the name *Histoplasma capsulatum* to round or oval bodies found in the endothelial cells and monocytes in certain cases of splenomegaly. This was found in autopsy material from patients in Panama.[1] In 1934, deMonbreun isolated the organism by culture from a clinical case and proved it to be a fungus.[2] Since 1934, much attention has been given to this disease, and we now identify the organism, *Histoplasma capsulatum,* as the sole etiological agent for this disease. Hodgson and associates[3] summarized 138 proved cases of histoplasmosis in 1950. In 65 of these cases there was reported to be pulmonary involvement. Forsee and co-workers[4] presented 30 cases of focalized pulmonary histoplasmosis following histopathologic examination. No recent tabulation of reported cases of histoplasmosis is available, but isolated reports of proved cases have markedly increased in recent years.

Various classifications of histoplasmosis have been presented. Conant, Smith, and others[5] present 3 distinct types: (1) primary histoplasmosis, (2) reinfection histoplasmosis, and (3) progressive histoplasmosis. Furcolow[6] is preparing to present a clinical classification based on symptomatology.

Since our series is composed primarily of pulmonary pathology, with only one focalized lesion, we will refer to the clinical form expressed by the term "chronic progressive pulmonary histoplasmosis" (as suggested by Furcolow). This clinical form could be classified under reinfection histoplasmosis, utilizing the types just mentioned. This type of histoplasmosis is of particular interest because of the similarity to chronic, progressive, cavitary tuberculosis, and we feel our experience substantiates this view.

Chronic progressive pulmonary histoplasmosis (reinfection type) was not assumed to exist until 1948 when Johnson and Batson[7] and Bunnell and Furcolow[8] presented original cases of pulmonary histoplasmosis with multiple

From the Department of Surgery, Missouri State Sanatorium, Mt. Vernon, Mo.
Read at the Thirty-fifth Annual Meeting of The American Association for Thoracic Surgery at Atlantic City, N. J., April 24 to 26, 1955.
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calcified areas in the lungs indicating healing. Sutliff and his associates[9] published cases similar to these and used the term "active chronic pulmonary histoplasmosis." Their patients presented calcifications in the lungs and cavity formations in the upper lobes, suggesting fibrocaseous tuberculosis. Sputa were negative for the tubercle bacillus, the tuberculin skin test varied, and the histoplasmin skin test was generally positive. Final proof in the diagnosis was established by finding the organism, *Histoplasma capsulatum.*

The Missouri State Sanatorium lies on the periphery of the endemic belt which includes the Mississippi and Ohio River Valleys and runs along the Appalachian Mountains. When numerous patients presented findings similar to those just described and pulmonary tuberculosis could not be proved, chronic progressive pulmonary histoplasmosis was suspected. Eighteen proved cases of pulmonary histoplasmosis have now been found at our institution. Seven patients have been subjected to surgery and 5 more were treated with MRD-112 (beta-diethylaminoethyl-fencholate).

MATERIAL

These 12 proved cases of chronic progressive pulmonary histoplasmosis form the basis of this report. Tabulation of some of the data as to the surgical and medical cases in this report shows a similarity to cases previously reported. Two of the 12 patients had pulmonary tuberculosis in addition to pulmonary histoplasmosis. Seven of the patients were submitted to surgery; 6 of these without drug therapy and 1 receiving MRD-112 for sixty days. The remaining 5 were treated with MRD-112. The ages ranged from 37 to 62. All were men except two; only one Negro patient was in the series. The duration of illness ranged from six to sixty-seven months. One patient gave a history of pulmonary disease for twenty-five years, but a diagnosis of histoplasmosis was not proved. The lesions were confined to the upper lung fields in 8 cases. In 4 cases there was bilateral pulmonary involvement. In 2 of these 4 cases, the disease had progressed to complete destruction of the left lung with apical infiltrations on the right. Eleven patients presented fibrocavitary disease and the other one presented nodular tuberculoma-like lesions.

All patients presented upper respiratory symptoms with the exception of the patient who presented nodular disease. This patient was completely asymptomatic. We considered the disease to be active because none of the patients could be employed at the time of admission to the hospital. All symptoms proved to be progressive; repeated x-rays revealed increased disease. Table I summarizes the surgical cases.

Five of the patients who survived surgery have returned to normal life. One patient died on the tenth postoperative day following a massive pulmonary embolus. One patient died sixty hours following left thoracotomy with acute pseudomembranous enteritis with toxic hepatitis and toxic nephrosis. The remaining 5 (to be reported later) are still hospitalized and are receiving aminostilbamidine or no drug therapy.

TABLE I. SURGICAL CASES OF HISTOPLASMOSIS
STATE SANATORIUM

NAME	AGE	ONSET	X-RAY FINDINGS	SKIN TEST		ORGANISM FOUND	LATEST HISTOPLASMIN SEROLOGY	LENGTH OF OBSERVATION (MONTHS)	TREATMENT AND COURSE
				TBC	HISTOPLASMIN				
S. R.	58	1/52	Multiple cavities, right lung	–	+	Histo + Sputum + Lung	C/F Test: 0 Prec. Test: 0	37	Right pneumonectomy; 18 mo. p.o. improved and working
E. M.	53	7/52	Cavity and infiltration, right lung	+	+	A.F.B. + Sputum Histo + Lung	C/F Test: 0 Prec. Test: 0	32	Dual segmental resection; 17 mo. p.o. improved and working
H. F.	41	10/53	Cavity and infiltration, RUL	–	+	Histo + Sputum + Lung	C/F Test: 0 Prec. Test: 0	18	Right upper lobectomy; 13 mo. improved and working
H. H.	37	9/53	2 inspissated cavities, left lung	–	+	A.F.B. + Lung Histo + Lung	C/F Test: 0 Prec. Test: 0	19	Wedge resection left side; 10 mo. p.o. improved and working
G. M.	46	12/53	Infiltration and cavity, RUL	+	–	Histo Lung	C/F Test: 8 Prec. Test: 40	6	Right upper lobectomy; 5/13/54, dead pulm. embolism—10 days
D. B.	43	10/53	Cavity, RUL	+	+	Histo Lung	C/F Test: 8 Prec. Test: 0	16	Right segmental resection; 8 mo. p.o. working
A. D. E.	56	12/48	Cavities, left lung; bilateral infiltration	+	+	Histo + Sputum + Lung	C/F Test: 32 Prec. Test: 40	67	MRD-112 experiment; left thoracotomy; dead

Histo = *Histoplasma capsulatum.*

REPORT ON CASES WITHOUT DRUG THERAPY

CASE 1.—S. R., a 59-year-old white woman, was first admitted to the Missouri State Sanatorium on Feb. 23, 1953 (Fig. 1). She stated that in January, 1952, she had had cough, hemoptysis, was easily fatigued, and had lost weight. The productive cough remained, weight loss was persistent, and the sputum remained streaked with blood on occasion. In January, 1953, she had symptoms consistent with cholecystitis. An x-ray of the chest revealed disease in the right lung, and she was advised by her physician to enter the Sanatorium. At the time of admission she had lost 20 pounds, had begun to have night sweats, and the cough and hemoptysis persisted. Mild dyspnea on exertion was noted.

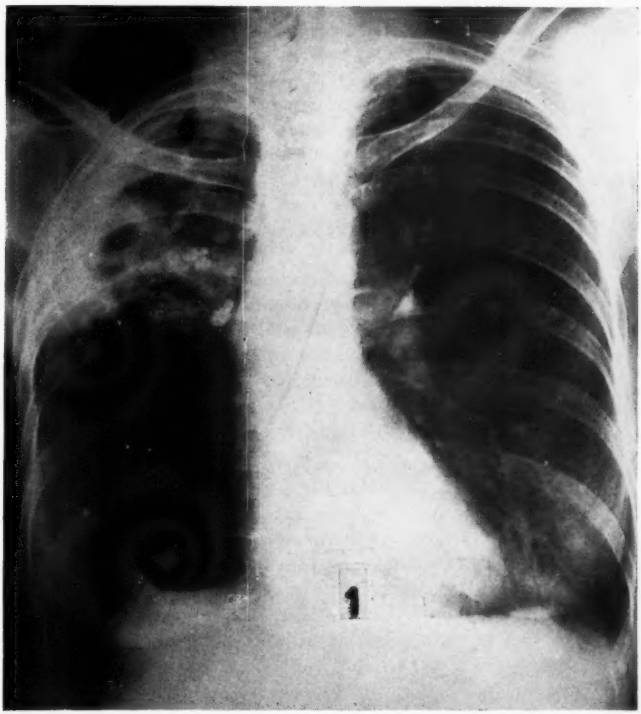

Fig. 1.—Case 1. A 59-year-old white woman with proved pulmonary histoplasmosis.

The family history and past history were noncontributory. Physical examination revealed a well-developed, chronically ill, white woman, showing signs of recent weight loss. Fine moist râles were heard over the right upper lung field. The blood pressure was 120/74. The remainder of the examination was not remarkable. Complete blood studies were normal. Repeated sputum examinations, including cultures, were negative for acid-fast organisms. Tuberculin skin tests, first and second strengths, were negative. Coccidioidin and blastomycin skin tests were also negative. Histoplasmin skin test was positive. The patient remained in the hospital as a diagnostic problem. Bronchoscopic examination, including smears for malignant cells and acid-fast organisms, was negative. On Sept. 23, 1953, a sputum culture was reported positive for *H. capsulatum*. Two days later, a right

pneumonectomy was performed. The patient had a relatively uneventful postoperative course. Cultures from the resected lung were positive for *Histoplasma capsulatum* and the organism was also identified in the tissues. Serologic studies prior to surgery were stable at 1:16 on the complement fixation tests. Ten days postoperatively the complement fixation titer rose to 1:32 and one month following surgery was 1:64. Since that time the strength of the reaction to the complement fixation test has declined and at the present time is 1:8, as are also the precipitin tests for histoplasmosis. The patient has now been followed for eighteen months and is completely asymptomatic. She has gained 20 pounds in weight and has returned to her duties as a housewife.

CASE 2.—E. M., a 53-year-old Negro woman, developed a productive cough, fever, chills, and weight loss in September, 1952. These symptoms persisted, and in December, 1952, she developed pleurisy on the right side. She was admitted to the Missouri State Sanatorium on Feb. 27, 1953. X-ray on admission revealed infiltration in the right upper lobe and the superior segment of the lower lobe with definite cavities in these locations. Physical examination was noncontributory except for moist râles over the right lung. Urinalysis and hemograms were normal. Smears and cultures were positive for acid-fast organisms, and a diagnosis of pulmonary tuberculosis, far-advanced, active was made. The patient was started on isonicotinic acid, hydrazide (INH), 4 mg. per kilogram of body weight, and streptomycin, 1 Gm., twice weekly. A pneumoperitoneum was instituted on April 14, 1953, and was discontinued Feb. 5, 1954. The sputum converted after three months of drug therapy. The tuberculin skin test was positive, as was also the histoplasmin test. On Oct. 21, 1953, the posterior segment of the right upper lobe and the superior segment of the right lower lobe were resected. The postoperative course was uneventful. Acid-fast organisms were not found in the resected specimen, but *H. capsulatum* could be demonstrated in the lung tissue. The patient was discharged on April 1, 1954, with two diagnoses: (1) pulmonary tuberculosis, far-advanced, arrested, and (2) pulmonary histoplasmosis, inactive. Sputum cultures have remained negative for both organisms since surgery, the serologic titer is negative, and the patient is working.

CASE 3.—H. F., a 41-year-old white man, developed a productive cough, malaise, and pain in the right upper chest in August, 1953 (Fig. 2). A diagnosis of "flu" was made by his local physician but, after the symptoms continued, an x-ray of the chest was made in November, 1953, and the infiltration and cavitation in the right upper lobe were found. He had a weight loss of 20 pounds in four months. He was admitted to the Missouri State Sanatorium on Dec. 2, 1953. Physical examination revealed only moist râles in the upper right chest. Otherwise, the examination was noncontributory. Routine laboratory studies were normal. Twenty sputum smears and three cultures failed to reveal acid-fast organisms. Bronchoscopy on Dec. 21, 1953, was negative. Skin tests were as follows: tuberculin, 3 plus; histoplasmin, 3 plus; blastomycin, 1 plus; and coccidioidin, negative. Sputum cultures were reported positive for *Histoplasma capsulatum.* Serologic studies revealed a complement fixation titer of 1:8. On Feb. 10, 1954, a right upper lobectomy was performed. The patient had an uneventful postoperative course and was discharged on March 17, 1954. Repeated cultures since surgery have failed to reveal *H. capsulatum.* The serology is now negative for histoplasmin. The patient has returned to his usual occupation of farming.

CASE 4.—H. H., a 37-year-old white man, dates the onset of his illness to September, 1953, when he had a routine chest x-ray made, and was told he had a shadow in the left lung. He displayed no symptoms referable to the chest. He was admitted to the Missouri State Sanatorium on Feb. 6, 1954. Admission x-rays revealed a solid lesion in the left lung field in the mid-portion which was interpreted as a tuberculoma or a neoplasm. Physical examination was noncontributory. Urinalysis and hemograms were normal. Tuberculin skin test was negative, but the histoplasmin skin test was strongly positive.

Bronchoscopy was not remarkable. Repeated smears and cultures were negative for acid-fast organisms and fungi. The patient refused surgery until a second admission. On April 26, 1954, a wedge resection of two tuberculomalike lesions was performed. Both lesions were located in the lower lobe. The postoperative course was uneventful. Frozen sections revealed a granuloma similar to tuberculosis. Consequently, the patient received streptomycin and para-aminosalicylic acid (PAS) immediately after surgery. Cultures from the specimen were reported positive for *H. capsulatum* and acid-fast organisms. The Schubert histoplasmin complement fixation and the Salvin histoplasmin precipitin tests were negative prior to surgery and have remained so since surgery. The patient has returned to work but we plan to continue antituberculosis therapy for one year postoperatively.

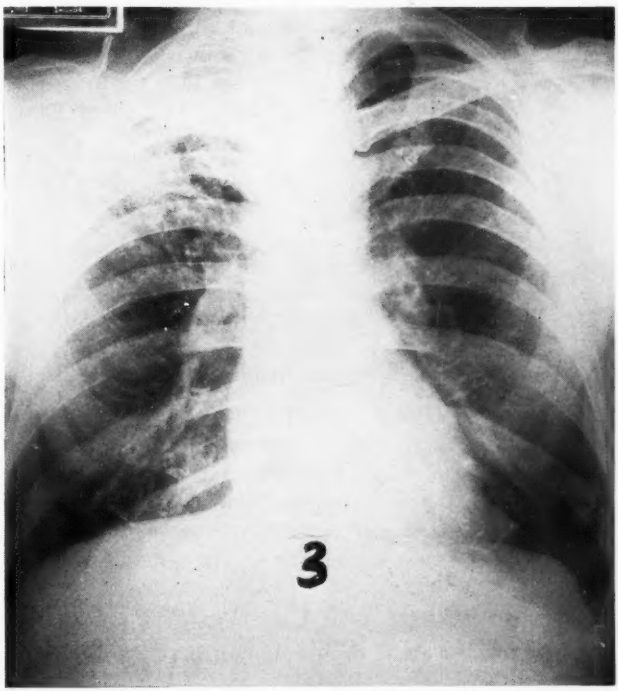

Fig. 2.—Case 3. A 41-year-old white man with proved pulmonary histoplasmosis.

Case 5.—G. M., a 46-year-old white man, had generalized aches, productive cough, and chills in December, 1953. A local physician treated him with penicillin, and after an x-ray of the lungs was made, he was admitted to the State Sanatorium on Jan. 4, 1954. X-rays of the lungs on admission revealed infiltration and cavitation in the right upper lobe. Physical examination revealed moist râles over the right apex, an amputated third finger on the right hand, and an inguinal hernia. Urinalysis and hemograms were normal. Skin tests were: tuberculin, 2 plus; and fungus skin test, negative. Twenty sputum examinations and three cultures failed to reveal acid-fast organisms. Sputum cultures for fungi were also negative. Complement fixation test for histoplasmosis was 1:8 and the precipitin test was 1:40 on May 7, 1954. On May 12, 1954, a right upper

lobectomy was performed. *Histoplasma capsulatum* was easily identified in the lung tissue. The patient was ready for discharge on the tenth postoperative day, when he became cyanotic, markedly dyspneic, and complained of a terrific pressure in the chest. The blood pressure and pulse could not be obtained. He died two hours later in spite of heroic therapy. Autopsy revealed a massive embolism of the main pulmonary artery.

CASE 6.—D. B., a 43-year-old white man, had a cough with streaked sputum in October, 1953. The blood-streaked sputum continued intermittently until an x-ray was made in the Outpatient Department of the Sanatorium. This showed a cavity in the right upper lobe and a suspicious area of cavitation in the left upper lobe. He stated that he also had a pleuritic pain in the right chest on occasion. Following his admission to the Sanatorium on Jan. 19, 1954, routine urinalysis and hemograms were normal. The physical examination was noncontributory. Three cultures and numerous sputum smears were negative for acid-fast organisms. Repeated complement fixation titers for histoplasmin demonstrated a rising titer from 1:4 to 1:16 over a four-month period. Sputum cultures failed to reveal *Histoplasma capsulatum*, however. On June 7, 1954, an apical-posterior segmental resection was performed. His postoperative course was uneventful. Tissue cultures were reported positive for *H. capsulatum* and negative for acid-fast organisms. He was discharged on June 22, 1954, and has returned to his farm. Repeated cultures for fungi have been negative since surgery and the complement fixation titer is now 1:8. Segmental resection of the cavitary lesion on the left has been recommended.

CASES TREATED WITH MRD-112

Six additional patients were proved to have chronic progressive pulmonary histoplasmosis by culture of the organism from the sputum. The severity of this type of disease and the similarity to cavitary tuberculosis suggested that if drug therapy were beneficial, surgical resection for destroyed lung components would be safer. The spread factor in the surgery of histoplasmosis can be compared to the spread which occurred in tuberculosis before the use of antituberculosis drugs. There was experimental evidence that the antifungus agent, MRD-112,[10] would be beneficial in this respect. This drug is technically known as beta-diethylaminoethyl-fencholate.* A dosage of 150 mg. daily, intravenously, was selected and first administered to 5 patients starting on June 1, 1954.

On Aug. 1, 1954, the case next presented was selected for a left upper lobectomy. X-rays of Cases 7, 8, and 12, who received MRD-112, are presented (Figs. 3, 4, and 5).

CASE 7.—A. E., a 56-year-old white man, was first seen in the Outpatient Department of the Missouri State Sanatorium in December, 1948, after a mobile unit chest x-ray revealed pulmonary disease. He was followed in the Outpatient Department through July, 1953. All sputum examinations were consistently negative for acid-fast organisms. He had experienced progressive dyspnea since 1945. In August, 1953, after cutting silage, he experienced a cough, productive of purulent material, fever, and chills. He received streptomycin and penicillin from his local physician. The streptomycin was continued for two months. On Oct. 5, 1953, he was admitted to the Sanatorium, with a history of weakness, fatigue, and a weight loss of 15 pounds prior to admission. Physical examination was negative except for moist râles scattered over the left upper lung field posteriorly. The blood pressure was 130/84. The admission x-ray revealed bilateral infiltration in the

*Produced by the Wm. S. Merrell Company.

apical portion of each lung. Several definite cavities were present in the left upper lung field. No definite cavities were seen on the right. All sputum examinations, including cultures, were negative for acid-fast bacilli. Bronchial smears were also negative for malignant cells and acid-fast organisms. Skin tests were: tuberculin, 3 plus; histoplasmin, 4 plus; blastomycin and coccidioidin, negative. Sputa were reported positive for *Histoplasma capsulatum* in December, 1953. Serum sent to Dr. Middlebrook for tuberculin complement fixation was negative. The patient had received INH and PAS from Oct. 23, 1953, to December, 1953, when the diagnosis of pulmonary histoplasmosis was established. He was discharged in December, 1953, to be followed in the Outpatient Clinic. Histoplasmin complement fixation was positive on April 1, 1954, at 1:128.

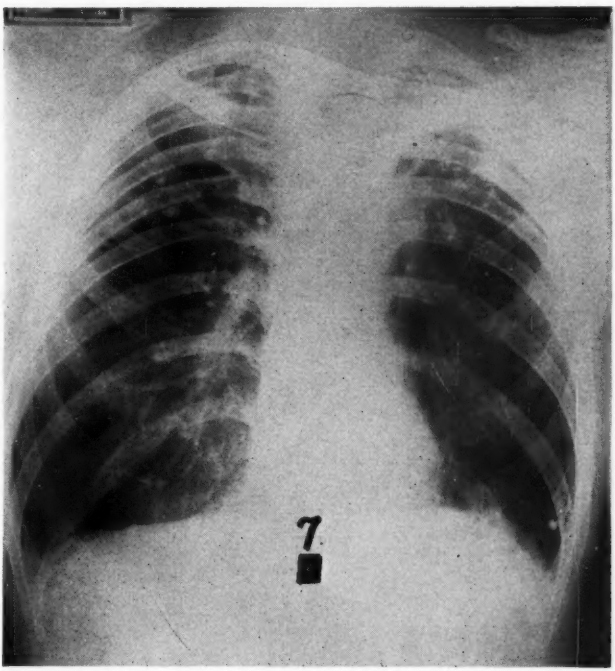

Fig. 3.—Case 7. A 56-year-old white man with proved pulmonary histoplasmosis.

On May 26, 1954, the patient was readmitted to participate in the controlled histoplasmosis study (Fig. 3). *Histoplasma capsulatum* was again cultured from the sputum on two occasions. Smears and cultures were again negative for the tubercle bacillus. Routine laboratory work-up and special liver and kidney tests were run. No evidence of liver or kidney damage was found, and the patient was started on MRD-112, 150 mg. intravenously daily, on June 1, 1954. Four other patients were started on this drug at the same time. After sixty days of therapy, with no obvious improvement, we advised a left upper lobectomy in an attempt to remove the cavitary components. On Aug. 13, 1954, a left exploratory thoracotomy was done. A large cavity with extensive reaction was found in the upper lobe; however, the superior segment of the lower lobe was markedly involved and the basal segments of the lower lobe were emphysematous and cystic. A pneumonectomy would have been necessary to remove the disease, and, with the infiltration in the right lung, we decided against this surgery.

Approximately four to six hours after surgery the patient showed signs of shock which did not respond to whole blood, Levophed, etc. Nine hours after surgery he vomited 3,000 c.c. of coffee-ground material. Drainage consisted of only 150 c.c. of blood into the thoracotomy bottles. He died in irreversible shock sixty hours postoperatively, after receiving 8 whole blood transfusions, with anuria for twenty-four hours. Permission for autopsy was obtained.

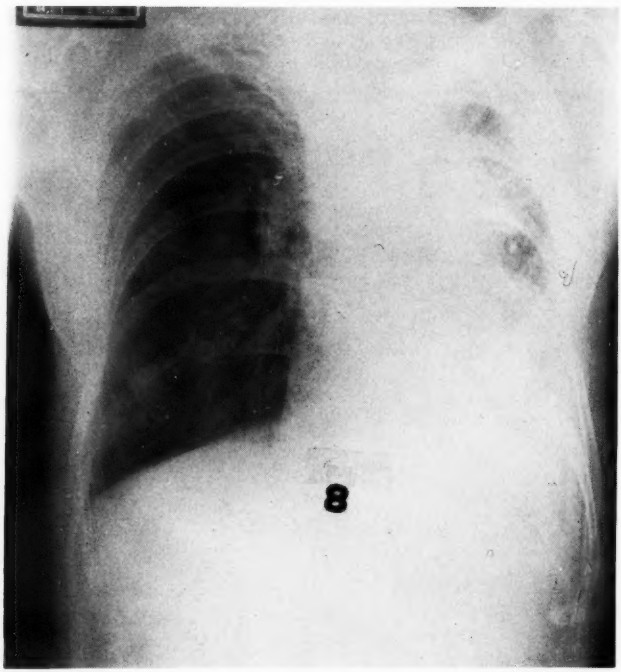

Fig. 4.—Case 8. A 67-year-old white man treated medically with MRD-112.

The pertinent findings from autopsy were: The parietal pleura on the left was markedly thickened and fibrous and there was an inflammatory reaction between the left lung and the chest wall. The middle segments of the left lower lobe presented a thin-walled emphysematous bulla. Throughout the lower lobe were numbers of discrete firm nodules. The superior half of the upper lobe and the superior segment of the lower lobe presented a large irregular density over which the thick pleura was noted. Beneath this pleura was revealed, on section, a thin-walled irregular-shaped cavity, measuring 3 cm. in longitudinal dimension. The inner wall was granular and reddish in appearance. The tissue around this was nodular, presenting numerous tiny cavities and, at the lower portion of the cavity, there was a communicating bronchus. The right lung showed numerous discrete, hard nodules which measured up to 8 mm. and were found to be present in the lower and middle lobes. There was marked infiltration throughout the upper lobe.

Gastrointestinal Tract: The stomach was somewhat dilated and contained approximately 250 c.c. of grayish-brown material. The mucosa lay free. The first portion of the duodenum contained bile-stained mucoid material. The jejunum and ileum revealed a

red, friable mucosa which could be easily scraped away. No discrete ulcerations were present. The cecum, ascending, transverse and descending colons were filled with dark, tarry stool which had the consistency of soft putty. The mucosa was intact and pale red in appearance.

Microscopic: Lungs: Sections from the area of the grossly described cavitary lesion revealed an irregularly outlined wall, the inner aspect covered with acidophilic-staining necrotic material. This overlay a zone of fibrotic reaction. The cells showed a tendency to picket-fence formation. Subjacent to this there was a loose fibrovascular area in which multinucleated foreign body giant cells and inflammatory cells were seen. Several bronchi showed disfigurement of the walls with desquamation of the epithelium. Tissue stained with acid-fast bacilli (AFB) and PAS stains failed to reveal the presence of acid-fast organisms or of intracellular inclusion bodies. Cultures taken from the cavity were positive for *H. capsulatum.*

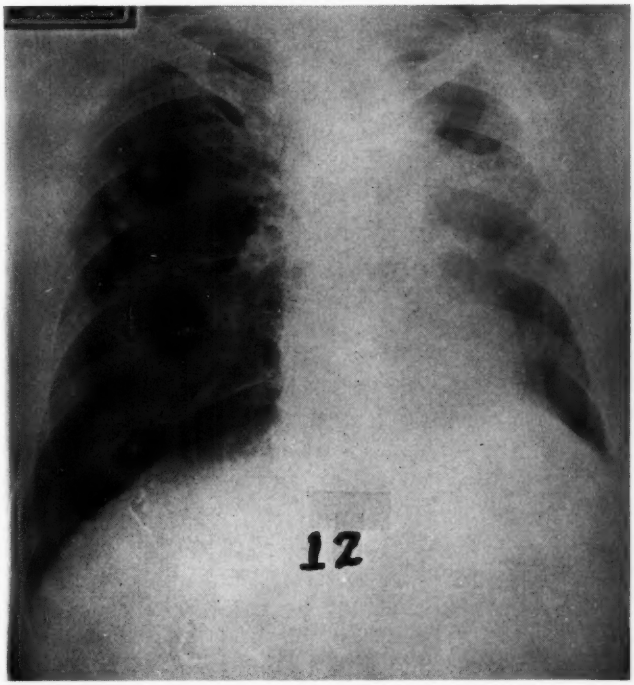

Fig. 5.—Case 12. A 61-year-old white man treated medically with MRD-112.

Liver: Sections showed extensive central and mid-zone parenchymal necrosis. The cells showed loss of nuclei, marked granularity, and swelling of the cytoplasm. The peripheral zones showed swollen liver cords and hyperchromatic nuclei.

Kidneys: Sections of the cortex showed very extensive degeneration of both the proximal and distal tubules. The glomerular tufts were moderately swollen and showed some amorphous deposit. Within some of the tubules was seen accumulation of slaty-gray deposit. The medullary portion presented moderate interstitial edema and the tubular epithelium appeared intact. The histologic features were those of nephrosis involving the corticotubular system.

Small intestine: Sections showed pronounced loss of granular epithelial mucosa. In some areas the villous processes had sloughed off and instead there was a hemorrhagic edematous inflammatory tissue. In others, the villous processes presented marked hemorrhagic extravasation. Throughout the wall there was much edema and numbers of eosinophils and neutrophils. The histologic feature was that of subacute enteritis.

Final Pathologic Diagnosis: (1) Acute pseudomembranous enteritis with toxic hepatitis and toxic nephrosis complicating irreversible postsurgical shock, and (2) pulmonary histoplasmosis, bilateral.

Following this tragedy, no further surgery on these patients was contemplated until long-term observation and study could be carried out. These cases will be published in detail later, but several observations concerning the drug, MRD-112, can be made at this time. First, no benefit has been observed in any patient with chronic progressive pulmonary histoplasmosis treated with MRD-112. One patient treated with this drug suffered a spread to the opposite lung three months after therapy. Two have shown increased symptoms of cough, hemoptysis, and weight loss. These two have also shown a marked rise in the serologic titer. All continue to have sputa from which *H. capsulatum* can be cultured, and 4 of the 5 remaining cases show varying degrees of liver degeneration, as proved by liver biopsy.

PATHOLOGY OF RESECTED AND AUTOPSY SPECIMENS

Puckett[11] reviewed the pathology in resected cases and was able to identify the organism, *Histoplasma capsulatum,* in 22 cases. Four well-defined groups were found, varying from a localized pneumonitis to a cavity with satellite tubercles. A survey of the pathologic findings in our series revealed only 1 case in which the lesion resembled an isolated nodule similar to a tuberculoma. In the remaining cases, all revealed cavities of varying size, from 2 to 5 cm. in diameter. Numerous smaller cavities were scattered around the periphery. The cavities contained caseonecrotic material and were lined by smooth friable walls. The inflammatory reaction extended to the pleura, creating a thickened fibrotic pleura which could not be separated from the underlying lung. An extrapleural resection was required in 6 cases. The pleura in Case 1 measured 1½ cm. in thickness.

On microscopic examination the cavities were found to be filled with cellular detritus and caseonecrotic material. The areas of necrosis were bordered by a zone of fibrocytic reaction containing fibroblasts, plasma cells, mononuclear macrophages, and foreign body giant cells. Single and conglomerate tubercle-like formations were observed and, in 4 of the cases, irregular-shaped refractile bodies were found within the giant cells. The bronchi within and adjacent to the cavities showed varying degrees of bronchiolitis.

Periodic acid-Schiff stains were a valuable aid in the demonstration of the fungi in tissues of 5 of our cases. Peabody and co-workers[12] have recently reported on the value of this stain in demonstrating fungi in tissues of pulmonary granulomas. These authors suggest that since fungi cannot be cultured from such small nodular lesions in many cases, this might represent the

healing phase of such disease. Furcolow,[13] in 1948, was of the opinion that organisms in calcified lesions might not be viable. We certainly would agree with this, but if a breakdown occurred, then a spread of the disease might occur similar to the spread which occurs after the sloughing of a tuberculous inspissated cavity.

SEROLOGIC STUDIES

Serologic studies have been carried out in detail on all patients by the U. S. Public Health Service, Kansas City, Kan., through the cooperation of M. L. Furcolow, M.D., Medical Director. All the resulting titers cannot be tabulated, but in Table II examples of the manner in which we have tried to utilize this data are shown. Until more experience is gained in the knowledge of serologic studies, caution in their interpretation must be used, but we feel certain facts have been gained.

TABLE II. SEROLOGY RESULTS

CASE 1. (S. R.)			CASE 9. (W. D.)			CASE 7. (D. E.)		
	HISTOPLASMIN			HISTOPLASMIN			HISTOPLASMIN	
DATE	CF*	PPT†	DATE	CF	PPT	DATE	CF	PPT
8/ 1/53	32	80	12/17/53	neg.	80	5/ 1/54	1:64	40
8/13/53	1:32	80	4/ 5/54	1:16	1:40	5/28/54	1:256	40
9/25/53	Operation		6/ 1/54	MRD-112		6/ 1/54	MRD-112	
9/28/53	16	80	6/11/54	1:8		6/ 5/54	1:32	40
10/ 2/53	16	80	10/22/54	32	100	6/22/54	1:32	40
10/ 6/53	32	80	12/17/54	1:32	100	7/23/54	1:16	
10/24/53	64	80	2/ 8/55		80	8/ 7/54	1:32	
5/21/54	8	40				8/13/54	Operation—died	
9/ 1/55	8	8						

The serology on S.R. is negative. The serology on W.D. has continued to rise since MRD-112 was administered. We feel this precludes surgery. The findings at surgery on D.E. revealed extreme activity. This was Case 7.

*Complement fixation.

†Precipitin.

We feel that the highest titers represent the highest degree of activity of the disease. Cases are considered positive and active when the titer is higher than 1:4 on either the complement fixation test or 1:10 on the precipitin test. It is from such patients that the organism has been isolated. A significant titer, using the yeast phase antigen, denotes early disease; whereas, chronic disease is suggested by a significant titer using the broth-filtrate antigen, histoplasmin. In an attempt to apply this knowledge as an aid in operative intervention, we now wait until a titer of 1:16 or less is obtained. Case 7 had a complement fixation titer of 1:32 and a precipitin titer of 1:40. Marked activity was demonstrated at autopsy, with positive cultures being obtained from the cavity in the left lung and from a hilar node.

Complete serologic studies have been utilized in an attempt to follow the postoperative cases. Four of the 5 have negative titers and 1 has a complement fixation level of 1:8. Should any case show a rise in the serologic titers, medical therapy in the form of MRD-112 or aminostilbamidine would be instituted, because we feel this would represent relapse or reactivation of the histoplasmosis.

DISCUSSION

The effects of medical therapy have been very disappointing in all forms of histoplasmosis. Christie and colleagues[14] reported that 5 of 12 patients with the disseminated form of the disease had recovered following treatment with ethyl vanillate. Other forms of therapy have included sulfadiazine, bacillomycin, Aureomycin, streptomycin, stilbamidine, isoniazid, and actidione. Chronic progressive pulmonary histoplasmosis, in spite of its insidious course, has never responded to any form of therapy either. Michael and Vogel[15] reported on the use of MRD-112 in the treatment of a disseminated case of histoplasmosis. Six cases of chronic progressive pulmonary histoplasmosis treated at the Missouri State Sanatorium with MRD-112 showed no response to this drug.

Pulmonary resection, as reported by several others,[16, 17] appears to offer progress in the therapy of pulmonary histoplasmosis. With the exception of coccidioidal disease, it has not been advocated widely for other pulmonary mycotic infections. Our experience confirms this concept and suggests several indications for resection.

Sutliff, Hughes, and their associates[9] stated as an indication for surgery: a localized lesion without evidence of tuberculosis. Pulmonary coccidioidomycosis and tuberculosis occurring as coexisting diseases do not seem to influence each other adversely.[18, 19] Our limited experience with tuberculosis and histoplasmosis suggests that these diseases do not affect each other alarmingly. We feel that if histoplasmosis and tuberculosis are localized together, and that if adequate antituberculosis therapy has been administered, resection is definitely indicated. We feel that a person weakened by chronic progressive pulmonary histoplasmosis and remaining in a tuberculosis sanatorium, with or without a diagnosis of tuberculosis, should receive antituberculosis therapy prior to resection.

The only spread to the contralateral lung in the 12 patients mentioned in this report occurred from a large cavity in the right upper lobe containing fluid. We had recommended resection, but the patient refused surgery. This bronchiogenic spread might have been avoided if the patient had accepted resection. We prefer to resect all cavities containing fluid in patients who have pulmonary histoplasmosis. In our opinion, this indicated resectional surgery.

Localized or circumscribed pulmonary lesions which remain undiagnosed warrant early thoracotomy. A period of six weeks for study and diagnosis seems warranted in selected cases. One of our cases in whom cancer was suspected fitted into this category, and both acid-fast organisms and *Histoplasma capsulatum* were found in the cultured tissues.

Even though 2 of the patients in this series had segmental resections and 1 had wedge resection, it is now our belief that lobectomy would be the operation of choice. Further follow-up studies and operative experiences will be needed before this final observation can be completely ascertained.

The role of collapse therapy in histoplasmosis, thoracoplasty or plombage, has never been studied thoroughly. In cases of chronic progressive pulmonary histoplasmosis, thoracoplasty prior to resection may be indicated in an attempt to stabilize the disease. We do not feel that thoracoplasty or plombage alone would have any beneficial effect on the type of disease which we have been observing at this hospital.

Last, if a drug becomes available which will protect the patient from a spread of the histoplasmosis or from a flare-up of stable disease, resection for destroyed areas of the lung would appear to be justified.

Follow-up examinations have been performed routinely on all resected patients. In all of the patients who survived surgery, the complement fixation studies have either remained stable or become negative. A rise in the serologic titer would indicate reactivation of the disease and medical therapy, such as MRD-112 or aminostilbamidine, would be given.

CONCLUSIONS

1. Medical therapy in chronic progressive pulmonary histoplasmosis has been disappointing. Six patients treated with MRD-112, a new antifungus agent, have shown no response to therapy.

2. Pulmonary resection appears to offer some progress in the therapy of chronic progressive pulmonary histoplasmosis. It has not been widely advocated and further experiences will be needed before final evaluation as to this form of therapy can be ascertained.

3. Pulmonary histoplasmosis and tuberculosis occurring as coexisting diseases are not uncommon. Antituberculosis therapy prior to resection, if the diseases are localized together, appears justified.

4. Serologic studies have proved to be of benefit in the preoperative preparations and postoperative follow-up of surgical cases. It is suggested that resection be withheld until the disease is stabilized as judged by the complement fixation test or until the strength of the reaction is 1:8 or less. Further observation with relation to the complement fixation studies is also necessary.

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Discussion

DR. J. W. PEABODY, JR., Washington, D. C.—As a guest of the Association, I would first like to express my gratitude for the privilege of the floor. Having incorrectly inferred from the title of this paper that we might be at odds about the merits of MRD-112 in treating histoplasmosis, I should apologize for rising to discuss Dr. Polk's splendid presentation, for it is apparent that we are all agreed on the relative ineffectiveness of this compound. Actually, our entire experience with the chemotherapy of progressive histoplasmosis has been most discouraging. Because of previous disappointments with any number of drugs exhibiting in vitro effectiveness superior to that of MRD-112, we were naturally somewhat skeptical prior to its use. The following case confirmed our doubts and is worth recording, since it provides the best possible evidence of its clinical inefficacy.

(slide) This is the admission chest roentgenogram of a 40-year-old white male patient from Dr. J. D. Murphy's service at Oteen, N. C., showing bilateral exudative disease with left apical cavitation. Sputum was repeatedly negative for acid-fast bacilli, but bronchial washings grew out *Histoplasma capsulatum* as did many subsequent sputum specimens.

(slide) Here following an interval of bed rest, note the general improvement although the cavitary disease in the left apex seems better defined. This patient then received 150 mg. of MRD-112 daily, for twenty-three days, only to have a follow-up roentgenogram (slide) disclose an extensive spread to the left lower lobe. Without further drug therapy the latter density subsequently cleared. He has since had a thoracoplasty and will probably require a lobectomy.

All of this simply illustrates that as yet we have not found a satisfactory therapeutic agent, unless of course the toxicity of nystatin can ultimately be circumvented.

While a great many other points might be mentioned, two in particular deserve emphasis, namely, the prevalence of histoplasmosis and its remarkable similarity to both primary and reinfection types of tuberculosis. It is fast becoming evident that regardless of one's geographic location, histoplasmosis will be recognized proportionately to one's interest and suspicion. For example, we now have resected over 50 pulmonary granulomas in more than one-third of which *Histoplasma capsulatum* can be demonstrated by special stains. (slide) This photomicrograph shows nothing more than caseation necrosis, a finding once considered prima facie evidence of tuberculosis. The same tissue section, however, after

decolorization and restaining by the periodic acid-Schiff method (slide) discloses myriads of *Histoplasma capsulatum*. This is not to imply that the method is new; it is simply incredible that it should be so slow in being accepted. Most pathologists still need to be coaxed into giving the PAS and Gridley stains a decent trial.

Finally, coexisting histoplasmosis and tuberculosis should not be overlooked, a situation we have encountered at least three times. (slide) This patient presented a cavitary lesion in the left apex. Sputum was positive for acid-fast bacilli. Three cavities were found in the resected specimen, but only one of these contained tubercle bacilli. The other two cavities, including the one visualized so nicely in this planigram, contained *Histoplasma capsulatum* in tissue sections and grew out *Histoplasma capsulatum*. Such findings emphasize the need for very careful evaluation of every granulomatous process.

The authors are to be commended for a very timely and stimulating presentation.

DR. FELIX HUGHES, Memphis, Tenn.—I hope if you have any lingering doubts that histoplasmosis is a separate entity, and an entirely different disease, that this paper and the discussion will help to dispel it. With a patient who appears to have tuberculosis but has never had a positive sputum, the probable diagnosis of histoplasmosis should be made. The figures presented in San Francisco from the Fitzsimons group were on resection of granulomas caused by histoplasmosis with little active disease. The prognosis is good at the onset of the disease, and the patient may not even be sick. Then it may give rise to multiple calcifications, and I think histoplasmosis is the cause of many of the calcifications that we have in the past attributed to pulmonary tuberculosis. I know you have seen the cavities that have been present with histoplasmosis in Dr. Polk's slides and Dr. Peabody's slides.

(slide) Here is another that was removed before the diagnosis was made. We recently had a patient with all the symptoms of an acute lung abscess, who was treated with all the antibiotics, and acute cavitary disease was found when the resected lesion was opened. The microscopic picture was that of caseous tuberculosis. However, instead of culturing tubercle bacilli, only the *Histoplasma capsulatum* grew on the culture media. At VAMTG Hospital (Kennedy Hospital) we have had 16 cases and we do not believe that MRD-112 is of great benefit. For cavitary lesions of histoplasmosis the complications of resections may be compared to resection of active open tuberculous cavitary lesions with bacilli resistant to chemotherapeutic agents as shown by Dr. Welles and his associates, in the first paper presented this morning. Dr. Murphy has 1 patient he thinks was cured by thoracoplasty, and some type of collapse procedure may be of benefit in treating patients with bilateral cavitary lesions.

I agree with Dr. Sutliff that the time appears appropriate to survey the patients under treatment for pulmonary tuberculosis to determine the incidence of pulmonary histoplasmosis both as a separate disease and as a complicating lesion. Routine culture for fungi of all resected pulmonary lesions is also recommended.

DR. SHELDON E. DOMM, Knoxville, Tenn.—East Tennessee has a high incidence of histoplasmosis, and the observation of cavitary lesions in our practice is not uncommon. One case undergoing resection may be worthy of a brief report.

The patient (G. E. H.) was a 45-year-old white man. X-ray showed a 2 cm. cavity in the left upper lobe. Tuberculin skin test was negative. Histoplasmin skin test was strongly positive. The sputum was negative for acid-fast bacilli but was positive for *Histoplasma capsulatum*.

The patient underwent segmental resection of the apical-posterior segments of the left upper lobe by Dr. W. K. Rogers. Pure culture of *H. capsulatum* was obtained from scrapings of the cavity lining. (Slide.) The pathologic report was histoplasmosis. The patient enjoyed an uneventful postoperative course, and follow-up seven months postoperatively shows no recurrence or complication. The patient did not receive MRD-112 or other specific chemotherapy.

We have recently observed bilateral thin-walled histoplasmosis cavities of three years' standing in a woman patient who had previously undergone right middle lobe lobectomy for bronchiectasis. Bilateral resection is contemplated.

We would like to stress the danger of overgrowth by *H. capsulatum* following indiscriminate antibiotic therapy in any patient from the endemic area of histoplasmosis. Certainly the routine use of prophylactic antibiotics postoperatively in cases of resection for histoplasmosis may be inadvisable.

DR. BUCKINGHAM (Closing).—In a diseased condition which so closely resembles chronic, fibrotic, cavitary pulmonary tuberculosis roentgenologically, the question has been asked how we suspect the diagnosis. In all hospital admittances, routine tuberculin and Histoplasma skin tests are done. If the histoplasma skin test is positive then further investigation is made from the serologic standpoint. This disease is not limited, or at least the types we have seen, by the normal anatomic barriers. It extends through the pleura into the intercostal spaces through the segmental planes and through the interpulmonary fissures, and it has been our thought that under these circumstances lobectomy certainly should be the procedure of choice. We have seen 1 case of the so-called solitary granulomatous lesion which the pathologist reported as granulomatous reaction; the acid-Schiff stain is almost specific in demonstrating the fungi in the tissues. We agree with the other discussants that the drug has not been of any great help.

When we first presented this paper for acceptance we thought we might have something of value in MRD-112, but as we got into the work more and more we realized that the drug was not of any specific help in this condition. Liver biopsies in all the cases treated with MRD-112 showed evidence of damage.

Dr. Crafoord asked what MRD is; it is an experimental drug which the Merrell Company has been working on. It has done a great deal of experimental work on fungus drugs.

THE DEVELOPMENT OF THE PLEURAL PARTITION TO PREVENT OVEREXPANSION OF THE LUNG FOLLOWING PARTIAL PULMONARY RESECTION

An Experimental Study With Clinical Application

Lyman A. Brewer, III, M.D., Angel F. Bai, M.D. (by invitation), and Wilfred M. G. Jones, M.D. (by invitation)
Los Angeles, Calif.

INTRODUCTION

EXTENSIVE resection of one or more lobes, or multiple segments of the lung, results in the creation of a large intrapleural dead space. If this space is not adequately eliminated at the time of operation, overexpansion of the lung leading to lung rupture, increase in the postoperative complications, prolonged postoperative morbidity, and finally decreased pulmonary function may result. The usual methods of controlling the space have certain inherent disadvantages. In searching for a more physiologic method, the concept of fashioning an intrapleural partition was evolved as a means of effectively preventing overexpansion of the remaining pulmonary tissue on the operative side. Experience with the production of 36 pleural partitions of various materials in mongrel dogs is presented along with the clinical application of this procedure.

EFFECT OF A LARGE INTRAPLEURAL DEAD SPACE ON REMAINING PULMONARY TISSUE

There is no question that if only a small pleural dead space is produced by the lobectomy the remaining lung tissue will expand to fill this cavity. It is especially true in children, where the alveoli apparently have not only the ability to distend but actually to increase in number. In adults, however, the lung generally expands by means of dilatation of the alveoli. This may progress to the formation of generalized emphysema or emphysematous bullae which so increase the residual air as to decrease greatly the pulmonary function of the unresected lung tissue. If significant amounts of pulmonary fibrosis are present in the remaining pulmonary tissue, dilatation of the alveoli is hampered and the lung expands but little. On the other hand, if considerable emphysema is present in the remaining lobe, then the expansion of this lobe to fill the pleural space results in the formation of large emphysematous blebs or bullae which further decrease the pulmonary function. In some instances, actual rupture of these emphysematous blebs may take place.

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If the residual lung does not expand to fill a large pleural dead space, immediately after operation, certain other mechanisms come into play. The diaphragm rises and usually is fixed. The mediastinum shifts to the affected side, provided firm mediastinal adhesions are not present. The chest wall contracts by narrowing of the intercostal spaces. Finally, pleural fluid is formed much as the so-called "fluid ex vacuo" in artificial pneumothorax, when a nonexpansile lung is present. These mechanisms all tend to decrease the pulmonary function on the operative side. However, of these mechanisms, the formation of large amounts of pleural fluid and the raised and fixed diaphragm most seriously depress the respiration of the remaining pulmonary tissue. In order to decrease the size of the pleural dead space after lobectomy, various operative procedures have been employed.

COMMON METHODS OF DECREASING PLEURAL DEAD SPACE

For over half a century a number of surgical procedures have been carried out to provide collapse of the lung in pulmonary tuberculosis. With the introduction of the antimicrobial drugs to destroy the tubercle bacilli and with the great technical improvements that have come with pulmonary resection, these collapse measures are now being used less and less as primary procedures. However, these collapse measures are still employed to decrease the pleural dead space following partial pulmonary resection. Diaphragmatic paralysis is the simplest and probably the most common method of decreasing this residual space. Once the diaphragm is relieved of its downward contraction, it will readily rise because of the positive intra-abdominal pressure and the negative intrapleural pressure, to obliterate even moderate intrapleural dead spaces. If the space is large, however, then this usually is insufficient and it may be necessary to add pneumoperitoneum. The latter alone is also done without actual paralysis of the diaphragm. This is effectual in obliterating small pleural defects. High levels of the diaphragm, however, cannot be immediately effected without phrenic paralysis or a previous extensive pneumoperitoneum. If the diaphragm is maintained for a long time at a high level in the thoracic cavity it becomes stretched and thin. Most of the contractility of the muscle fibers is then lost. The weak and thinned-out diaphragm cannot contribute greatly to the dynamics of respiration and there is a corresponding decrease in pulmonary function on the operative side. Thus, the simplest means of controlling the dead space in the pleural cavity may result in permanent loss of diaphragmatic action which may greatly decrease the pulmonary function.

The performance of thoracoplasty to collapse the chest wall has long been a common means of controlling the pleural dead space following lobectomy. This is an effectual method of closing this cavity and has the advantage of not impairing diaphragmatic function on the operated side. It has been used for many years throughout the civilized world and probably is the most generally accepted method of managing large pleural defects, especially in pulmonary tuberculosis. The mortality is low and it is a highly successful operation. However, the drawbacks are well known. First, is the deformity of the thor-

cic cage as well as the prolonged pain and discomfort that so often accompany this operation. Of course, the more limited the extent of the thoracoplasty, the less deformity and disability. However, if five ribs or more are removed, then the shoulder disability and pain may be troublesome. Second, the muscle imbalance and pain may severely decrease the functional capacity of the operated side, even though the diaphragm has not been molested. Certainly all thoracic surgeons, who have grown up in the thoracoplasty era and have had an appreciation of the discomfort, deformity, and loss of respiratory function which the patient suffered in order to be well, have felt the need for a simple, effectual and safe technique to take its place.

Since the beginning of this century, surgeons have inserted various foreign body prostheses into the extrapleural and pleural planes, as means of providing pulmonary collapse for active pulmonary tuberculosis. More recently this technique has been used to decrease the pleural dead space following pulmonary resection. Although a host of substances have been tried, there are a few which apparently are quite well tolerated by the body. Among them are paraffin, methyl acrylate (Lucite), zirconium, and Ivalon sponges. The advantages of these foreign bodies are that they are light in weight, can be easily inserted, and do not produce a great deal of foreign body reaction. The disadvantages which are well known are those inherent with the introduction of foreign material in any amount into a body cavity or an artificially produced space. The use of foreign body plombage as a treatment of pulmonary tuberculosis has given way to the safer thoracoplasty and pulmonary resections in most clinics throughout the world. Following World War II, Lucite sphere plombage, introduced by Wilson and Baker,[15] gained some popularity as a prosthesis material to provide collapse in pulmonary tuberculosis. However, after considerable experience, the nonspecific and tuberculous infections that occurred in the spaces about the Lucite spheres have made surgeons hesitant to employ these spheres as permanent prostheses, although we believe this form of treatment still has its advocates. The writings of Trent,[11] DesForges and associates,[8] Wada,[12] and others emphasize the dangers of this material when used as a prosthesis. Plastic sponge (Ivalon) first used by Grindlay and co-workers[10] has been further reported by Gale and associates.[9] The latter workers have reported satisfactory results in 46 out of 50 cases; however, Brantigan,[2] Davis,[7] and Charbon and Adams[5] have reported a number of infections. We have used the Ivalon sponge as a prosthesis in the extrapleural plane in dogs. Because of the infections that were so produced we have not employed it in humans. Since the report by Gale and co-workers,[9] in 1952, we have been unable to come across a similar series of cases. Thus, experience with this type of sponge has not been extensive enough for one to have a final opinion regarding its use at this time. It may be, with improvements in sterilization and in the management of the space, that this, or some other foreign body, may be well tolerated. However, as Clagett[6] has stated in his comments on Gale's paper, there has been considerable disappointment with other foreign bodies used in human tissues in the past, nevertheless further trial of this method was justified.

THE DEVELOPMENT OF THE PLEURAL PARTITION

We have not been completely satisfied with the techniques of thoracoplasty, phrenic operations, and pneumoperitoneum, and the filling of the extrapleural or pleural spaces with considerable amounts of foreign body material. For some time we have been searching for a simple surgical procedure that would be safe and effectual and that could be carried out immediately following the lobectomy and yet preserve the respiratory function of the remaining lung tissue on the operative side. It occurred to one of us (L. A. B.) that it might be possible to divide the pleural cavity into two compartments: One containing the remaining lung, which could then function in a normal manner, freed of the disadvantages of overexpansion, extensive collapse of the chest wall, and the paralyzed attenuated diaphragm. The second compartment, isolated by the partition, would be nonfunctional and would gradually fill with fluid and fibrin clot. By fashioning the partition across the upper portion of the pleural cavity a nonfunctional apical space would be created whereas the excursion of the diaphragm and lower ribs would not be impaired.

Therefore, to test out this concept of limiting pleural expansion, a series of 36 partitions were fashioned of various substances in mongrel dogs and the dogs were sacrificed at periods from one week to five and one-half months (Table I). The technique employed is the following: Under intratracheal ether anesthesia, lobectomy of one or more lobes was performed by the individual ligation technique. The bronchial stump was covered with a pedicled pericardial fat graft, according to techniques that we have previously reported both for experimental animals and humans.[3, 4] The pleural partition was then fashioned out of various substances and inserted into the pleural cavity.

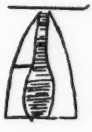
TABLE I. TYPES OF PLEURAL PARTITIONS IN EXPERIMENTAL ANIMALS

PARTITION	NUMBER	DATE OF POSTMORTEM EXAMINATION
Tantalum mesh	7	35 to 148 days
Steel mesh	8	48 to 300 days
Nylon mesh	6	20 to 176 days
Fascia lata	15	7 to 180 days
Total	36	7 to 300 days

First, woven mesh of tantalum and stainless steel wire was used. Then about one year later, when on the basis of our clinical experience we decided that wire mesh should not be used, we started to employ nylon and then autogenous fascia lata to fashion the partitions. Following the removal of the lobe or lobes of the lung, the remaining lung tissue was inflated to maximum expansion by positive pressure applied through the intratracheal tube. The partition was then sutured in place at the level of maximum pulmonary expansion to divide the pleural cavity into two compartments. This partition was usually fixed at the level of the fourth to sixth rib. In the case of the partition formed with the woven wire mesh, the screen was fixed to the chest wall by interrupted silk sutures leaving a space from 2.5 to 3 cm. along the medi-

astinum to prevent trauma to the heart and great vessels from the mediastinal displacement occurring with respiratory and cardial movements. Either pleura or a pedicled pericardial fat graft was used to bridge the defect. In the case of the partitions formed with the woven nylon and the fascia, these partitions were fixed to the mediastinal tissues and/or pericardium, as well as to the chest wall. Following the fixation of the pleural partition, the chest wall was closed in layers with interrupted cotton sutures. Temporary closed catheter drainage of the inferior pleural compartment was maintained during closure to expel all the air present and expand the remaining pulmonary tissue. The catheter was then withdrawn. All dogs survived the surgery with the exception of 1 animal which died before the experiment could be completed, apparently from faulty action of the anesthetic machine. The dogs were then examined periodically to observe the fate of the partition and the secondary effects on the intrathoracic organs.

TABLE II. FATE OF PLEURAL PARTITION IN EXPERIMENTAL ANIMALS

Type of Partition	No.	Complete	Incomplete	Displaced Upward	Pleural Membrane
					
Tantalum mesh	7	3	4	7	7
Steel mesh	8	3	5	8	8
Nylon mesh	6	5	1	0	6
Fascia lata	15	15	0	0	15
Total	36	28	10	15	36

FATE OF THE INTRAPLEURAL PARTITION

What happened to the intrapleural partition is summarized in Table II. Chest roentgenograms of the dogs with various types of partitions are shown in Figs. 1 to 4. It was noted that the wire screen partitions were complete in 9 out of 15 instances, probably because no firm fixation was made between the wire screen partition and the mediastinum. Furthermore, the wire screens tended to be displaced upward. The lung herniated up a little into the superior compartment in those cases where the partition was incomplete. The woven cloth partitions, however, were complete in all but 1 case. There was little tendency toward the upward displacement and no contraction or pull on the mediastinum was noted. In one instance the cloth partition was partially free in the superior space.

The autogenous fascia lata partitions were complete in all instances. There was no upward displacement. The partition was firm and strong with some pull on the mediastinum. The partition did show signs of contraction after the first month which was as much as from 20 to 50 per cent in three or four months. In no instance did the fascia partition pull free from the chest wall or mediastinum. There was no breakdown of the fascia so it formed an effectual barrier to prevent pulmonary expansion. All partitions were covered with a glistening membrane regardless of type of material used to form the partition.

Fig. 1. Fig. 2.

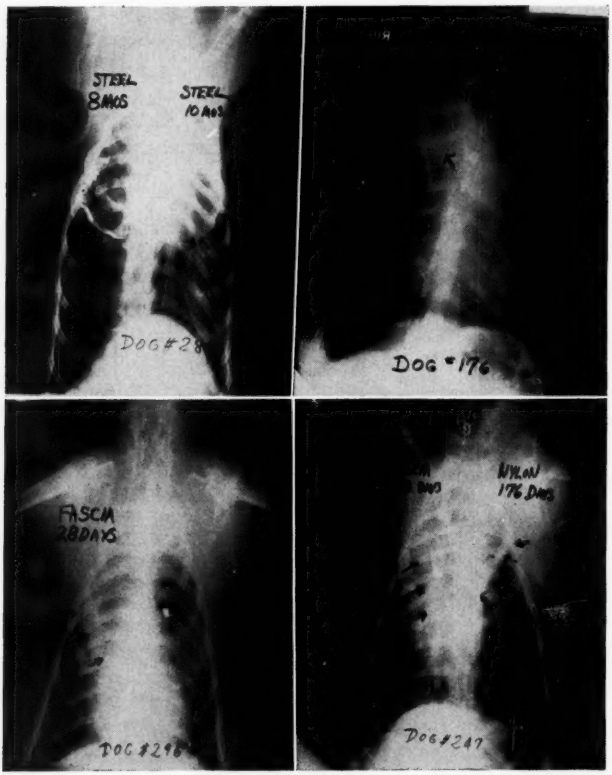


Fig. 3. Fig. 4.

Fig. 1.—Dog 285. Chest roentgenogram of bilateral steel mesh partitions (right side) eight months and (left side) ten months after upper and middle lobe lobectomies. The lower pleural compartments are clear. Upper compartments cloudy. Partial herniation of lung on right through incomplete partition.

Fig. 2.—Dog. 176. Chest film with nylon partition 118 days after right upper and middle lobe lobectomy. Right lower pleural compartment clear. Slight mediastinal shift toward upper compartment which is cloudy. Partition complete.

Fig. 3.—Dog 296. Chest x-ray fascia lata partition 28 days after upper and middle lobectomy. Clear lower pleural compartment. Upper compartment hazy. No mediastinal shift. Partition complete.

Fig. 4.—Dog 247. Chest film of bilateral upper and middle lobe lobectomy with right fascia lata partition 63 days after surgery and left nylon partition 176 days after operation. Lower pleural compartments are clear. Upper compartments cloudy.

MICROSCOPIC STUDIES OF THE FASCIA PARTITIONS

At the beginning of our use of fascia lata to form the partition in dogs there was considerable speculation as to the fate of these rather large grafts. Smaller grafts had been used for years in hernias and plastic operations and larger ones for chest wall defects.[15] Therefore, microscopic studies were carried out on these partitions beginning one week after the transplant to the pleural cavity up to five and one-half months. In one week's time (Fig. 5) the fascia lata was well preserved in the center of the partition between two layers of organized granulation tissue, two to three times the thickness of the fascia, containing an active fibroblastic proliferation with numerous capillaries and vascular spaces. There was a mild inflammatory reaction as evidenced by a sparse small round cell and neutrophil infiltration and a fibrinous exudate on the surface. Two weeks after transplant (Fig. 6) the granulation tissue was more densely fibrous although the fibrocollagenous fascia lata was well preserved in some areas. In others, replacement of the fascia with this fibrous granulation tissue had taken place. Inflammatory reaction was minimal.

In six weeks' time (Fig. 7), the original fibrocollagenous fascia was demonstrable as a narrow band in the center of the partition. This was integrated with the granulation tissue, which was now of dense fibrous and fibrocollagenous character. There were numerous capillaries and small blood vessels supplying the partition. These apparently arise from the parietal pleura and the adherent lung. The fascia lata fibers made up only about one fourth of the thickness of the partition which was composed of adult connective tissue with only a sparse infiltration with small round cells. After two months' interval (Fig. 8) the partition was entirely composed of a dense fibrocollagenous connective tissue of mature cells. It was impossible to distinguish between the original fibrous tissue of the fascia lata and that of the newly formed replacement fibrous tissue. It was a tough living tissue that had developed its own blood supply. Observation up to five and one-half months' time have shown no change in the microscopic findings just described for the two-month sections. Therefore, these studies reveal that the fascia lata remains viable for a period of about six weeks' time after which it becomes completely replaced with an adult fibrocollagenous connective tissue which, having its own blood supply, is a living fibrous partition. In one instance where the partition was formed with nylon mesh, the nylon had separated from the chest wall and was lying partially cured up in the superior space. However, a tough fibrinous membrane separated the pleural compartments.

OBSERVATIONS ON THE SUPERIOR PLEURAL COMPARTMENT

In animals with all types of partitions there was a slight shift of the mediastinum to the resected side and the intercostal spaces over the superior pleural compartments were somewhat contracted. Though the fragile mediastinal pleura was found to be tented and displaced to the operated side we do not believe there was any functional impairment of the structures of the mediastinum. Observations were made up to six months' time. Regardless

Fig. 5.

Fig. 6.

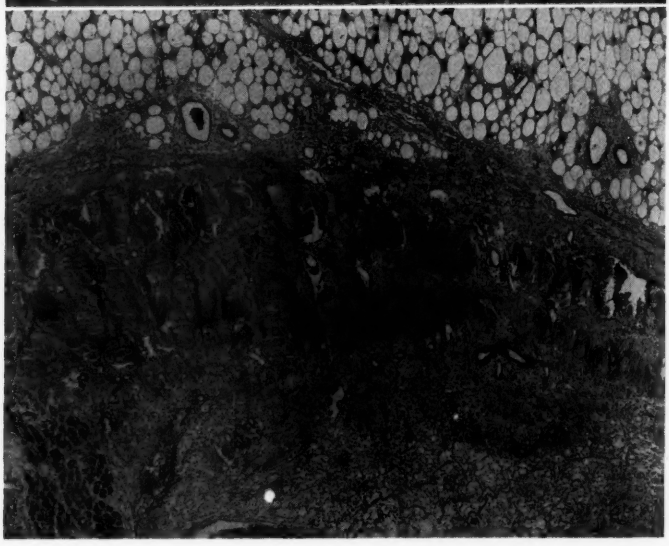


Fig. 5.—Dog 299. Fasca lata partition one week after transplantation. Fibers of fascia well preserved covered on each side by an organized granulation tissue made up of an active fibroblast proliferation with numerous vascular spaces and capillaries. Mild inflammatory reaction present.

Fig. 6.—Dog 264. Fascia lata partition two weeks after transplantation. Fascia viable, but is being replaced by a densely fibrous granulation tissue with numerous capillaries. Adipose tissue clinging to graft along superior border and a small bundle of muscle fiber in lower left-hand corner are well preserved.

Fig. 7.

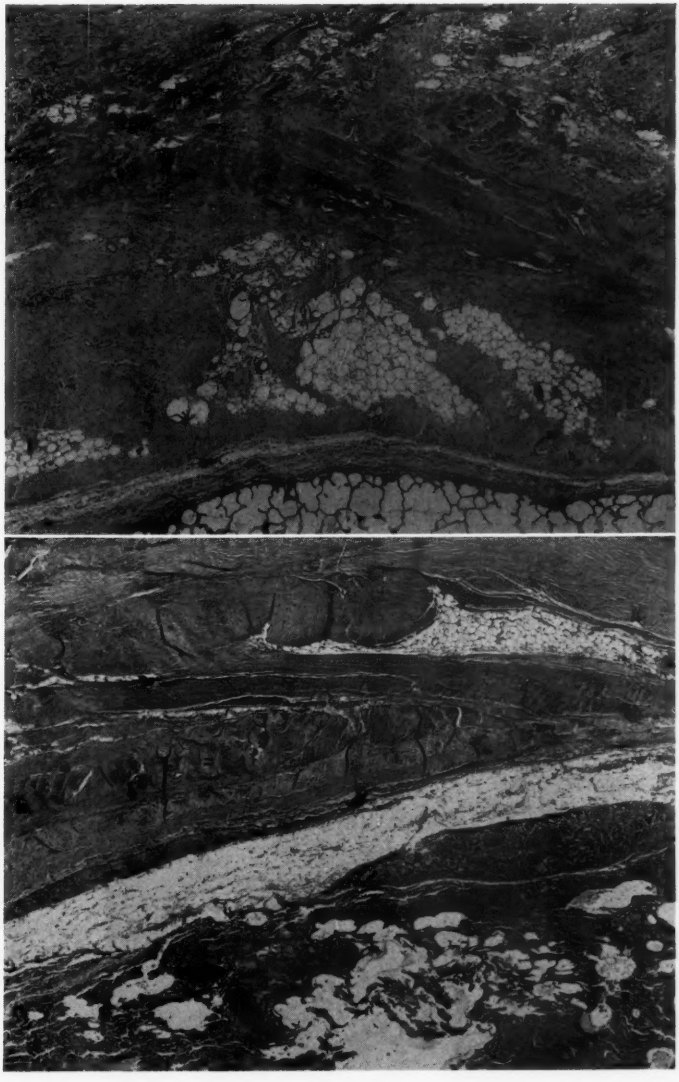


Fig. 8.

Fig. 7.—Dog 299. Fascia lata partition six weeks after transplantation. Fascia appears as a narrow band of fibrocollagenous tissue in center of partition. Adult connective tissue replacing fascia makes up most of partition. Fat cells and sparse muscle bundles still present. Thickened pleura and lung seen along inferior border of partition.

Fig. 8.—Dog 266. Fascia lata partition two months after transplantation. Partition now composed of mature fibrocollagenous connective tissue. Newly formed connective tissue cannot be told from original fascia layer. Scarred pulmonary tissue where lobar fissure had been incomplete is seen along inferior border.

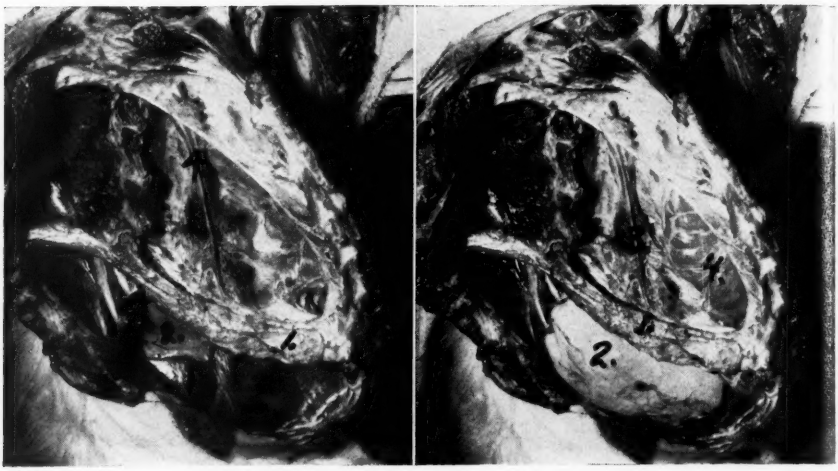


Fig. 9. Fig. 10.

Fig. 9.—Dog 295. Twenty-two days after right upper and middle lobectomy with fascia lata partition. View, right lateral thorax, bony cage removed. Upper and lower compartments seen from above. Fascial partition (*1*) intact. In lower compartment collapsed lower lobe (*2*) resting on smooth diaphragm (*3*), which is normal. Upper compartment divided by phrenic nerve (*4*).

Fig. 10.—Dog 295. View of right lateral thorax same as Fig. 9, with right lower lobe expanded with positive pressure on intratracheal tube. Note how right lower lobe (*2*) expands normally to fill lower pleural compartment below partition (*1*). Phrenic nerve (*3*) and anterior mediastinum (4) visible in superior compartment.

Fig. 11.—Dog 295. View of inferior pleural compartment showing fascial partition seen from below (*1*), collapsed lung free in the inferior pleural space (*2*), glistening diaphragm (*3*), and anterior mediastinal pleura (*4*).

of the material used to form the partition the superior space was completely lined with a shiny membrane in all instances where the pleura was complete.

EFFECT ON THE PLEURA AND LUNG IN THE INFERIOR INTRAPLEURAL COMPARTMENT

The most gratifying observation made in these experiments was the condition of the pleura and the diaphragm in the inferior pleural compartment (Figs. 9, 10, and 11). Except for adherence of the superior aspect of the lung to the pleural partition, there was complete absence of any pleural adhesions in the inferior space. Most important was the freedom of the diaphragm from any adhesion or clot whatsoever. This permitted the diaphragm to move in a normal manner. Parietal pleura and chest wall showed neither fixation nor scar, so that maximal chest wall movement apparently was also preserved. This meant that, so far as the remaining lobes of the lung were concerned, maximum expansion and compression of this pulmonary tissue was preserved. This preservation of pulmonary function was borne out by the clinical observation of the dogs which showed no lack of activity, even though in about one half of the cases they had received bilateral lobectomy with only the lower lobes on each side remaining for the function of respiration. As far as the remaining pulmonary tissue was concerned, there was no evidence of pulmonary tissue was concerned, there was no evidence of pulmonary emphysema. Microscopic examination showed the alveoli to be normal and similar to that of normal alveoli before surgery. These findings are most significant, and point to the fact that the intrapleural partition had achieved the purpose for which it was intended, with preservation of pulmonary function in the remaining lung.

CLINICAL APPLICATION

Although this paper concerns itself mainly with our experimental investigation that has been going on for a year and one half, the early results in human beings should be mentioned. To date our clinical experience is limited to the use of this procedure on only 9 cases (Table III). With the success of the wire mesh in chest wall replacement in humans and armed with our experience in dogs, we began to make a clinical trial of this technique using tantalum mesh about one year ago. Our first 5 cases did very well and we thought that this was the answer to the problem. In the next 2 patients, who were exceedingly bad risks (Cases 6 and 7), a secondary infection developed in the superior pleural compartment. With the occurrence of the secondary infection, we stopped employing the pleural partition operation clinically and turned to the laboratory again to find new materials out of which to form the partitions. We believed it was the material out of which we were fashioning the partition and not the principle that was at fault. After six months' experimenting with nylon and autogenous fascia in experimental animals we became convinced that of all the materials used, autogenous fascia lata was the most satisfactory one to form the partition. We were encouraged by the fact that the large fascia lata grafts used by Watson and James[14] to close chest wall defects had proved successful and

apparently were well tolerated. Our application of the fascial graft relied on blood supply coming in from the pleura of the chest wall, and mediastinum; in their use of the fascia new blood vessels developed from the overlying muscles.

TABLE III. CLINICAL EXPERIENCE

CASE	DIAGNOSIS	OPERATION	PARTITION	DIAPHRAGM	INFECTIONS SUP.	INFECTIONS INF.	MONTHS	RESULT
E. C. 43 M	TB	R U L	T. M.*	Ex.	No	No	12	Working
B. N. 39 F	TB	R U L	T. M.	Ex.	No	No	12	Working
H. W. 39 M	TB	R U L	T. M.	Ex.	No	No	3	Died; coronary
B. B. 29 F	Bronchiectasis	L L L Lingula	T. M.	Ex.	No	No	10	Working
O. H. 40 F	Cyst	L L L	T. M.	Ex.	No	No	7	Working
R. S. 70 M	CA	L L L	T. M.	Ex.	+	0	7	Space sterilized; working
C. C. 37 F	TB	R U L R M L, and D L L	T. M.	Ex.	+	0	10	Apical cavity; working
D. B. 55 M	TB	R U L D L L	Nylon	Ex.	0	0	First day	Died; pulmonary embolus
K. H. 55 M	TB	R U L S M L S L L	Fascia	Ex.	0	0	1	Early OK

*T.M. = Tantalum mesh.

And, so during the past month we have again started employing the partition operation in human beings, using fascia lata with success in one case. The early results were excellent but long-time observations are not available. It will be noted for the entire series that the results were excellent in all patients surviving surgery with the exception of 1 case. In 2 cases in which the partition was formed out of wire mesh, a secondary infection had developed in the superior pleural compartment. It was of interest that in both cases the lung completely filled the inferior pleural space and the pleura, lung, and diaphragm were not involved. Furthermore, a limiting membrane rapidly formed to encase both surfaces of the wire screen which completely isolated the infection in the superior compartment from that of the inferior space. Both these patients were extremely poor risks and we believe they would not have tolerated either thoracoplasty or phrenic crush with an extensive pneumoperitoneum to fill a huge dead space. In both cases the infection was drained several weeks after surgery, when the patient's condition had stabilized. In one instance it was possible to sterilize the superior pleural space with antibiotics so that the drainage tube could be removed. The patient now has a solidly healed chest wall and there is no evidence of infection in the superior space. He is well and working as a cab driver. In the second case, in which we classify the result as only fair, the cavity is slowly decreasing in size. It is now about 30 c.c. However, the patient's pulmonary condition was so poor that, in spite of the infection in the superior pleural space, we believe that the preservation of the vital basal segments of the lower lobe of the right lung saved the patient's life, for the contralateral lung was

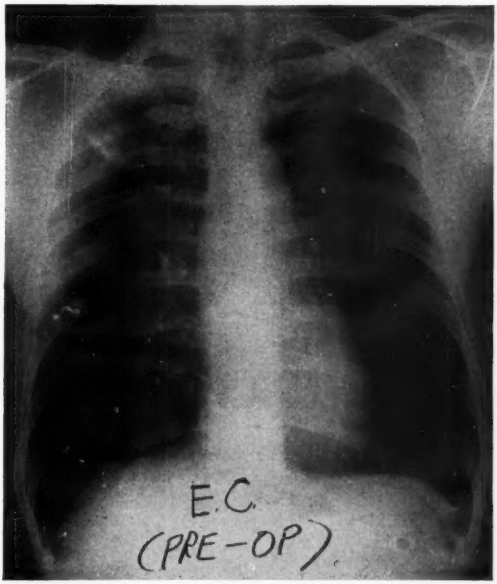


Fig. 12.—Case 1, E. C. Preoperative chest film. Pulmonary tuberculosis, right upper lobe. Bilateral pulmonary emphysema.

Fig. 13.—Case 1, E. C. Posteroanterior chest film one day after operation. Right upper lobe lobectomy with tantalum mesh partition to fourth rib anterior and fifth rib posterior. Lower pleural compartment, right, is clear. No fluid in upper compartment.

Lateral view shows position of tantalum mesh partition in relation to expanded middle and lower lobes. Note fissure between middle and lower lobes.

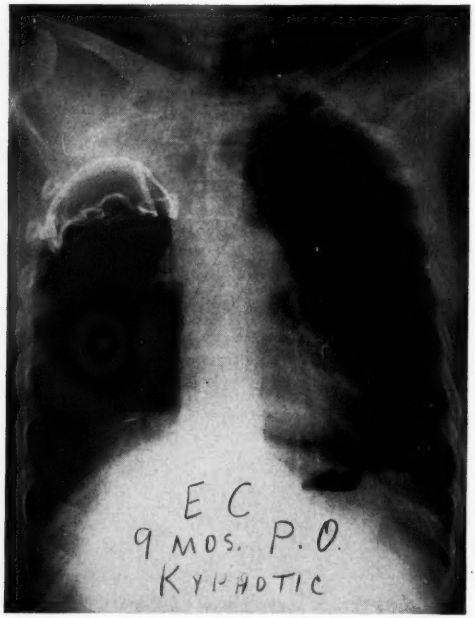


Fig. 14.—Case 1, E. C. Special kyphotic posteroanterior chest film months after operation. Note central bulging of partition and clear diaphragmatic angles.

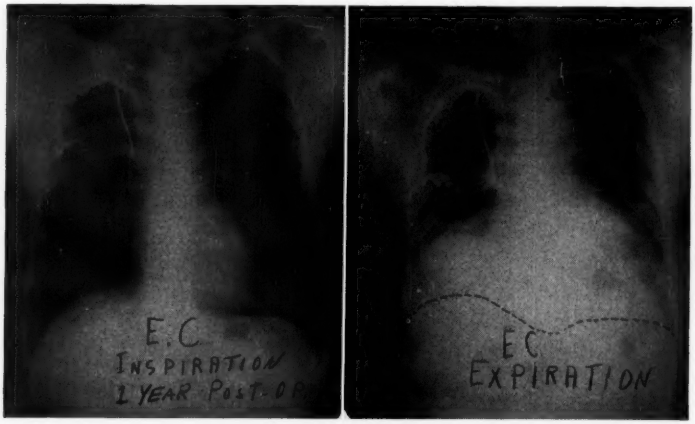


Fig. 15.—Case 1, E. C. One year after operation. Posteroanterior view on inspiration shows diaphragm at eleventh rib. On expiration the diaphragm rises two and one-half inches. Diaphragm action marked; contour completely free of adhesions or pleural reaction.

practically functionless from fibrosis, permanent diaphragmatic fixation, and marked postpneumothorax pleural thickening. She desperately needs the remaining portion of the right lower lobe of the lung to carry out respiration. We believe the patient would not have survived an extensive thoracoplasty, or paralysis of the right diaphragm following the multiple lobectomies on the right. Because of the steady clinical improvement and decrease in the pleural space, we have delayed in the removal of the superior wire mesh screen and the performance of a limited thoracoplasty, which she now can tolerate from the point of view of pulmonary function.

The excellent results of pulmonary function in the other cases, especially Case 1, with pulmonary tuberculosis (Figs. 12, 13, 14, and 15) and Case 5, with an extensive emphysematous cyst of the lungs cannot be overlooked. In Case 5, no other form of surgical procedure which is commonly used today to decrease the pleural space would have been satisfactory. The vital capacity is increased from around 1,100 to 2,200 following surgery, and the patient is no longer bedridden and is now doing her own housework.

DISCUSSION

As far as the experimental evidence goes in the 36 partitions made in dogs, the results were excellent without any infection. This fact alone commends this procedure for further clinical trial. The pleural partition prevented overexpansion of the lung with the preservation of function of the diaphragm and chest wall movement on the operated side. Thus, we believe that this procedure is more physiologic than diaphragmatic paralysis with or without pneumoperitoneum or thoracoplasty. Wade[13] has recently made an elaborate study of the role of the thoracic cage and diaphragm in respiration. His investigation showed that the diaphragm contributed 75 per cent of the ventilation of the lung while the chest wall contributes the remaining 25 per cent. The diaphragmatic movement in quiet respiration is 1 to 2 cm. but may increase to 7 to 13 cm. with deep breathing. He showed the chest circumference in quiet respiration to increase from 1 to 2 cm. while with severe effort it may enlarge from 5 to 11 cm. For six to eight months after birth, respiration is almost entirely diaphragmatic, from which time on the chest begins to contribute to the ventilation of the lung. Although Best and Taylor[1] believe that diaphragmatic motion contributes only 60 per cent to ventilation as compared to the 75 per cent reported by Wade,[13] the preservation of the function of this structure is of tremendous importance to the poor risk patient.

The physiologic function of the apex of the lung is much less than that of the middle and lower portions, due to the lack of motion of the apices with respiration. Therefore, we believe that it is important to make the functionless compartment at the apex. In lower lobe lobectomy, by freeing up the hilus of the upper lobe of the lung, it is possible to form an apical compartment without undue torsion or poor drainage from the displaced upper lobe bronchus. Thus the ventilatory effect of the diaphragm and lower chest wall on the lung is preserved, for the upper lobe can then function like a lower lobe. This was done successfully on 3 dogs and in 3 of the patients.

The drawback of the partition operation is the possibility of infection in the superior space. Whether this will prove to be greater in the series of patients with fascia lata partitions than is found in simple lobectomy remains to be seen. From our limited experience we believe it would be higher in a large series with wire mesh partitions. The fascia lata has the advantage of becoming completely replaced by a living fibrocollagenous connective tissue with its own blood supply from the pleura of the chest wall and mediastinum. If an infection develops in this space above a fascia partition, simple drainage with or without a subsequent limited apical thoracoplasty, should solve the problem. Experience has shown that wire mesh usually must be removed in the presence of infection, and we plan to do this eventually in Case 7. The 2 cases in which there was a pleural infection differed from the ordinary postoperative generalized empyema in that the infection was limited to the superior compartment and the lower compartment was completely filled with lung tissue and remained uninfected. Thus the diaphragm and chest wall action was preserved even though an apical empyema developed. Furthermore, a late, limited thoracoplasty, we believe, can be tolerated by these extremely poor risk patients when the function of the remaining lung has returned to a near normal level.

SUMMARY

1. The concept of the formation of the pleural partition to prevent overexpansion of the lung has been presented.

2. Experience with the formation of 36 such partitions in dogs is recorded.

3. The operation was shown to be successful in the experimental animals.

4. Fascia lata was proved to be superior to tantalum, steel mesh, and nylon cloth as a material to form a partition.

5. The advantages of this procedure lie in the prevention of the overinflation of the remaining lung without sacrificing diaphragmatic and lower chest wall function.

6. The disadvantage lies in the possibility of localized infection of the superior compartment. However, this localized infection may not be as disabling as a generalized postoperative empyema.

7. Only limited application has been made (9 cases) in patients with huge pleural dead space, following lobectomy.

8. Early clinical results would indicate that further trial of this procedure is justified using fascia lata to form the partition. This trial should be restricted to those cases with a large intrapleural dead space.

We should like to express our appreciation to Florence Rhudy, M.D., for her assistance in the pathologic studies on the pleural partitions and to Lester Gibson, M.Sc., of the Hunterian Laboratory for technical assistance with the animal experiments.

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DISCUSSION

DR. JOHN W. BELL, Sunmount, N. Y.—I think Dr. Brewer should be complimented on this fascinating contribution to the problem of intrathoracic space following resection surgery for tuberculosis. The use of a partition may be very helpful when such a space exists, particularly in the problem where the parietal pleura has been destroyed in mobilizing the upper lobe.

We have had experience with 25 pleural tents of the type described this morning. Our technique is similar to that described by Miscall and Klopstok and shown to you in their excellent movie. The pleural tents, or caps, have been fashioned at the time of operation at the conclusion of the resection. They have been very convenient in avoiding temporary space problems where they could be anticipated. I should like to make several technical points about these tents. Of course the pleural cap depends on the integrity of the parietal pleura. Where the pleura has been damaged by mobilization of the upper lobe it may be necessary to use a partition of some of the prosthetic materials selected by Dr. Brewer. All of our tents have been made from the parietal pleura. Occasionally there is a small rent in the pleura and air will leak up from the intrapleural space, even though it is drained with two tubes, into the extrapleural space above the tent. This may produce a tension pneumothorax which will dissect into the tissues and give alarming subcutaneous emphysema. This possible accumulation of air must be watched for and it may be necessary to decompress the extrapleural pocket with a third tube. The tent has been very useful in our hands in avoiding transient space problems.

No evidence has been presented today or in the literature that I know of, that tents, or even thoracoplasties for that matter, prevent overexpansion. Disregarding the fact that overexpansion has, we think, little to do with reactivation of residual tuberculosis, the overexpansion that the surgeon is trying to prevent may, of course, already have occurred when the surgeon enters the chest. Contracted segments co-exist with hyperinflated segments or lobes, so that nature has anticipated the surgeon in many instances.

We think these tents or partitions should have wider application in avoiding space problems in resections for tuberculosis.

DR. EDGAR DAVIS, Washington, D. C.—I rise for two comments only, first, regarding the use of Ivalon sponges and, second, about the present author's so-called "pleural tent." As you may recall, several years ago in discussing Dr. Joseph Gale's paper on

Ivalon sponges, I issued a word of warning about the hazards of this prosthesis. Inasmuch as it continues to be used, I would like to report that we have now completely abandoned its use. Almost all our patients in whom it was used have got into trouble, some as long as three and four years afterward.

Second, a number of years ago we started to do a procedure called an extrapleural apicolysis for the purpose of preventing overexpansion of the partially resected lung. It is interesting to see the same procedure now proposed as a new idea under the descriptive term "pleural tent." I feel that the bad results obtained from extrapleural apicolysis were due to the fact that a plombage was introduced at the time of surgery. Following lobectomies we soon learned that if we merely pulled the pleura down as was described this morning and sutured it in much the same manner as the present authors describe, we could obviate complications by deferring the introduction of a plastic prosthesis for a week or ten days. Then a small incision could be made in the apex, the fluid and fibrinous exudate removed and the space filled with Lucite spheres. So far as I recall we have used this in some 60 patients and have so far had no reason to regret it.

DR. BREWER (Closing).—I wish to thank the discussants for their remarks. Their expression of the dangers of the use of large amounts of foreign body material in the extrapleural and intrapleural planes certainly reflects an experience that is widespread today. We have tried to use parietal pleura to form the partition. Pleura is usually fragile and will not hold the suture so that this material has been unsatisfactory in our hands. A thickened or inflamed pleura once freed from its blood supply might be the source of infection. The problem of drainage is exceedingly important. We employ two drainage tubes both anteriorly and posteriorly and can see where three might be advisable. One must be careful to place one of the drainage tubes at the extreme apex of the inferior pleural compartment whether they be placed anteriorly or posteriorly. In some instances two should be placed at the apex of the pleural compartment if there is leakage of air from an emphysematous lung. The drainage of fluid has not offered a serious problem. This is probably true because the lung completely fills the inferior pleural compartment to seal off this space, provided the air has been adequately removed by suction. In some of the early cases we did have air passing up into the superior pleural compartment with the result that subcutaneous emphysema occurred. The proper placement of the drainage tubes and constant negative suction will prevent this.

The dangers of use of tantalum mesh is well taken. As pointed out in the paper, we have abandoned the use of this material to form a partition, and now use fascia lata. In the 2 patients with a superior compartment in which tantalum mesh was used, there was no general pleural infection. The inferior compartment was free of infection and the function of the diaphragm, lower chest wall, and remaining lung was preserved. This was lifesaving in the woman who was depending upon the basal segments of the right lower lobe for respiration with a poor functioning contralateral lung. We doubt if she would have survived a generalized pleural infection.

However, infection is the only drawback that has been observed to date in this method, and the operator must be careful with the preoperative preparation of the patient, the operative technique, and the postoperative care, to prevent such infection. From a physiologic point of view this method to our knowledge preserves the pulmonary function on the side of the resection better than any other procedure currently used. At the present time we are undertaking studies to demonstrate just how successful this preservation of pulmonary function is. The advantage of fascia lata lies in the fact that it is not a foreign body, that it is completely absorbed and a living membrane takes its place. Even though one might encounter an apical infection in the superior compartment, simple drainage would probably take care of it in most instances, with a limited apical thoracoplasty the maximum that would have to be done. In several cases in which we have used the pleural partition, where thoracoplasty or phrenic paralysis of the huge pneumoperitoneum were contraindicated, we wondered what we would have done had not the technique of the pleural partition been available.

OPERATIVE THORACIC DUCTOGRAPHY

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ALBANY, N. Y.

INTRODUCTION

SUBSEQUENT to the first effective intrathoracic ligation of the thoracic duct by Lampson[9] in 1946 to control chylothorax, an increasing number of similarly successful surgical experiences have been reported.[1, 2, 3, 8, 11, 13, 16, 17, 20] Since the primary concern of the present article is not with the historical aspects of chylothorax nor its etiology, diagnosis, mortality, or experimental studies, the reader is referred to the many excellent investigations and reviews which have appeared in the literature.[2, 4, 8, 9, 10, 13, 18, 19] The purpose of this communication is to present the results of anatomic studies of the thoracic duct system as well as to record our experiences with a radiopaque technique for visualization of the thoracic duct at the time of its deliberate surgical interruption in the treatment of chylous effusion.

Demonstration of the thoracic duct by contrast roentgenography is neither a new nor an original concept. According to Seannell,[15] it was suggested by Churchill and successfully accomplished by their group in a dog with excellent delineation of the thoracic duct. Emerson[7] in 1947 excised a supradiaphragmatic thoracic duct cyst and at operation injected the cyst with Diodrast, obtained a portable film, and proved communication of the cyst with the thoracic duct cephalad to it. Caudad injection was not performed. Anatomic studies of the thoracic duct in fresh post-mortem subjects by such radiopaque techniques have also been reported.[5] Touroff and Seley[20] instilled Lipiodol into the mediastinum following excision of a mediastinal hygroma for chronic chylothorax. Apparently no attempt was made by them to cannulate and visualize the duct, the Lipiodol being employed to promote an inflammatory response and subsequent fibrosis of any residual lymphatic radicles not ligated. These observations suggested to us that routine radiopaque visualization of the thoracic duct system at the time of operation might prove a valuable adjunct to the surgical interruption of the thoracic duct by exposing accessory ducts to ensure their recognition and subsequent identification and division at the diaphragm. No reports advocating such use of the technique herein described have been found.

MATERIALS AND METHODS

In thirty instances, the thoracic duct has been studied by proximal and distal injection of radiopaque dye at the level of the diaphragm. The dye was

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Read at the Thirty-fifth Annual Meeting of The American Association for Thoracic Surgery at Atlantic City, N. J., April 24 to 26, 1955.

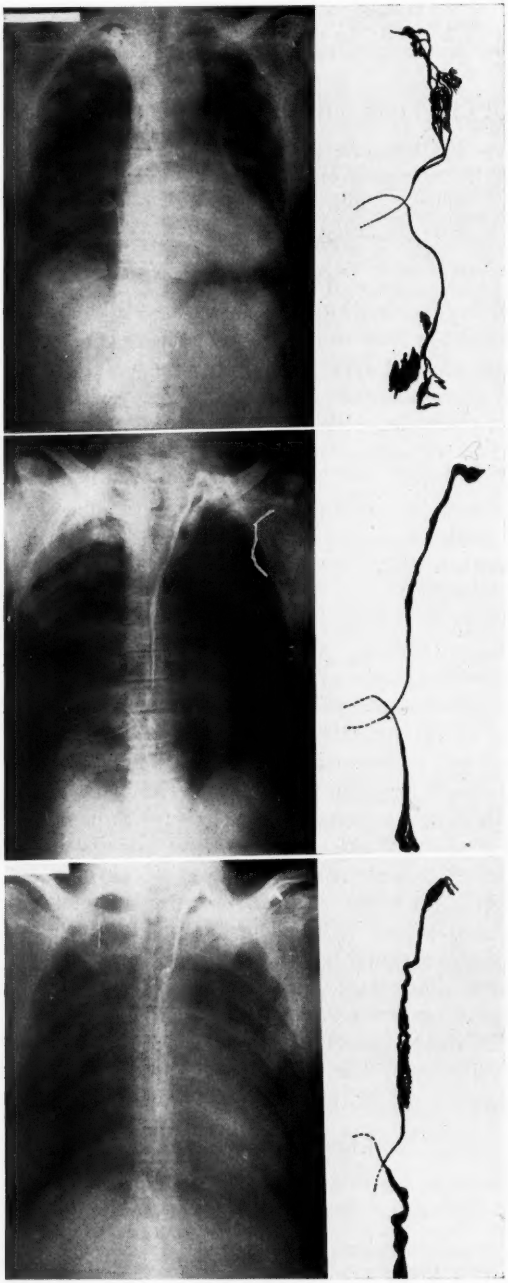
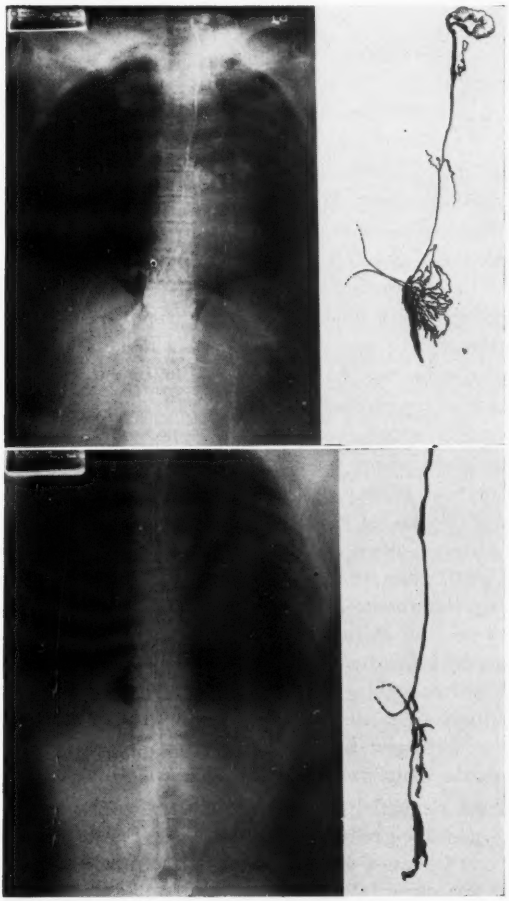


Fig. 1, *A*, *B*, and *C*. *(For legend see opposite page.)*

introduced by means of small plastic catheters with which both ends of the divided duct had been cannulated, and after the injection of 5 to 10 c.c. of dye both cephalad and caudad, one or more radiographic exposures in anteroposterior projection were obtained. In 27 cases these studies were performed on fresh post-mortem subjects by utilizing 50 per cent sodium iodide solution. In the remaining 3 cases, observations were made at the time of surgery by an essentially similar technique save that 70 per cent Diodrast or Urokon was utilized. Following anesthetization, the patients were placed in either the



D.

E.

Fig. 1.—Anteroposterior films of autopsy specimens following proximal and distal injection of 50 per cent sodium iodide solution into the thoracic duct at the level of the diaphragm. Line drawing of duct system is to right of corresponding film. *A*, Complete right-sided drainage. Insula in midthorax. Single trunk at diaphragm. Group I. *B*, Single duct throughout thorax. Group II. *C*, Left-sided drainage. Insula in midthorax. Single trunk at diaphragm. Group III. *D*, Many trunks at diaphragm. Low insula. Group IV. *E*, Double duct at diaphragm. Group V.

supine or lateral position over a portable Potter-Bucky diaphragm and exposures made immediately following injection of the dye. In 2 operative cases (Cases 1 and 2), methylene blue was injected prior to the radiopaque dye in an effort to identify the site of chyle leakage. In all the autopsy specimens, methylene blue was injected after the x-ray exposures were taken in order to facilitate identification and dissection of the duct system. The ducts were then dissected out following removal of the thoracic and abdominal viscera. Histologic examination of the cisterna chyli and various portions of the duct were undertaken and correlated with the over-all pathologic findings.

ANATOMIC FINDINGS

A brief review of the literature concerning the anatomy of the thoracic duct seems indicated at this time since diametrically opposed observations led us to pursue additional anatomic studies. That the thoracic duct is subject to considerable variation has long been recognized. Indeed, Winslow[22] in 1775 noted that the thoracic duct "is sometimes double, one on each side, and sometimes accompanied by pampiniform appendages." Rouviere[14] also noted the many variations reported in the literature and stated that articles dealing with its variations exceed those devoted to its "normal" anatomy. Davis,[6] in 1915, carefully studied the thoracic duct in 22 cases and described many variations which in conjunction with those previously reported by others led him to classify such variants into general categories which he felt were not only explainable but predictable on the basis of the embryology of the thoracic duct system which is early represented as a bilaterally symmetrical system and thus potentially bilateral throughout its entire course. Of special interest is his finding of two or more major ducts at the level of the diaphragm in approximately 33 per cent of cases. In contradistinction to these observations are those of Van Pernis[21] who, in a study of 1,081 autopsy specimens, categorically stated that the thoracic duct was always represented as a single duct below the level of the eighth thoracic vertebra. The results of Celis and Porter[5] utilizing a technique similar to the one employed in the present study, tend to support the findings of Van Pernis, although it is to be noted that in only two instances was the duct injected in a retrograde manner at the diaphragm, all others being injected only in a cephalad direction. In our opinion, this factor vitiates their findings since the roentgenographic recognition of double or collateral channels at or below the diaphragmatic level requires such retrograde filling to demonstrate their presence.

In the 30 cases studied by us, the anatomic variations could be classified according to five general groups which correspond closely to the categories of Davis. In only one instance was the duct entirely right-sided (Group I). In 9 cases the duct was essentially single throughout its course (Group II). In 10, the duct was single at and below the level of the tenth thoracic vertebra, although there was a double duct or "insular" pattern in the upper thoracic region (Group III). In 5, many channels were noted at the diaphragm with an essentially single representation above. These we have classified as having a low insula (Group IV). In the remaining 5 there were two distinct ducts

at and below the level of the tenth thoracic vertebra (Group V). Representative examples of these five categories are illustrated in Fig. 1 and a summary of the anatomic findings is depicted diagrammatically in Fig. 2.

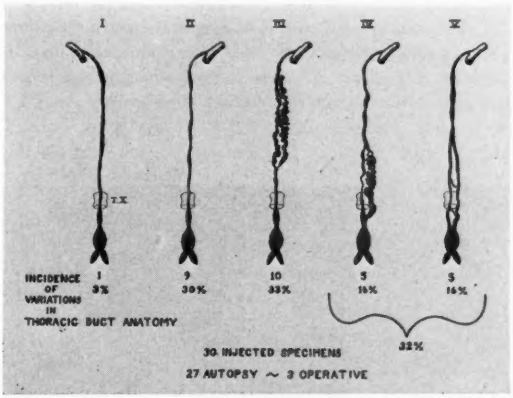


Fig. 2.—Summary of anatomic findings in thirty injected specimens classified into five general groups.

In order to assess a possible causal relationship between the variations noted and malignant disease, the pathologic diagnoses, available in all cases, were correlated with the anatomic findings. It was found that in the first three anatomic groups totaling 20 subjects, 10 (50 per cent) had neoplastic and 10 nonneoplastic disease. Of the former, most cases were far advanced with massive generalized metastases causing death. In Groups IV and V consisting of 10 subjects, 2 (20 per cent) had neoplastic disease, and the remaining 8 (80 per cent) died of nonneoplastic disorders. Continuing study of the anatomy and pathology of the thoracic duct is still in progress and will form the basis for a more detailed report in the future.

CONCLUSIONS

From the foregoing observations, certain pertinent conclusions seem inevitable. First, that contrary to the findings of some[5, 21] the thoracic duct may be represented at the diaphragmatic level by two or more major trunks. Second, that evidence thus far does not suggest that malignancy, even though widely disseminated, is necessarily the cause of such variations, since 80 per cent of the double duct systems at low levels were not associated with malignant disease. That malignancy may cause some increase in lymphatic channels is suggested in 1 case of lymphoma (Case 3) discussed below.

Our observation that roughly one third of thoracic ducts have two or more trunks at the level of the diaphragm is obviously of practical significance in the surgical treatment of chylothorax, and a satisfactory method of recognizing such ducts at the time of operation would appear to be of distinct value. The following case reports are presented as examples of a satisfactory method to achieve this end.

CASE REPORTS

CASE 1.—G. A. S., a 57-year-old white woman, was first admitted to the Albany Hospital on Nov. 12, 1952, with a complaint of increasing dyspnea of seven months' duration, associated with low-grade fever, but no weight loss. For three months prior to admission, the patient had had weekly thoracenteses with relief of the dyspnea but no apparent abatement in the rate of fluid formation. Physical findings revealed a thin, emaciated, chronically ill-appearing white woman, whose vital signs were within normal limits. She was moderately dyspneic and orthopneic. Significant findings were limited to the thorax where there was evidence of bilateral pleural fluid, and to the neck and axillae where palpable nodes were

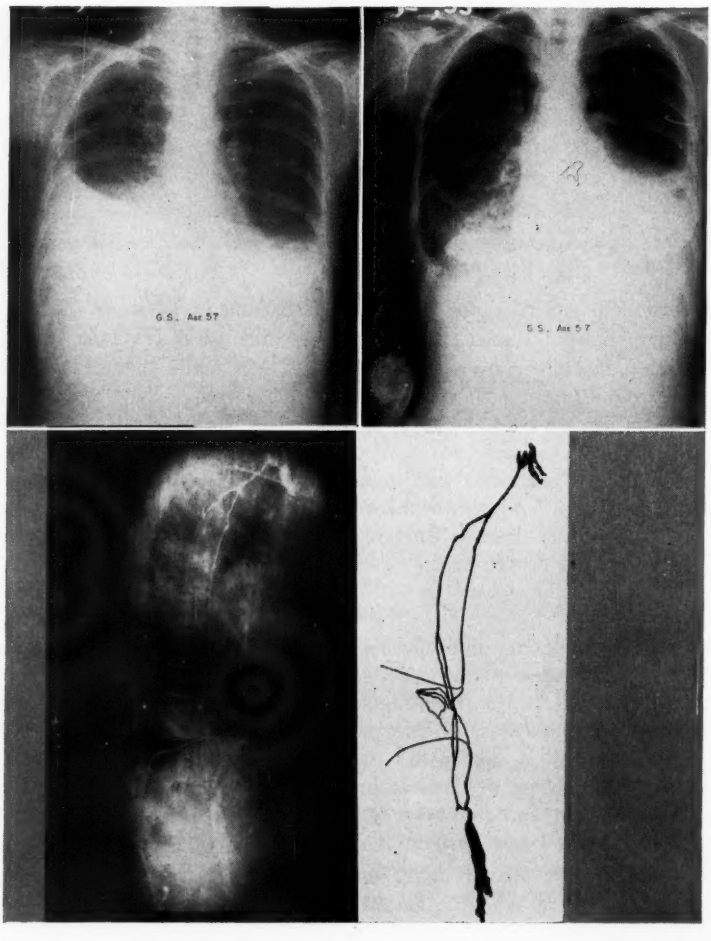


Fig. 3.—Case 1. Bilateral chylothorax in 57-year-old woman with lymphoma. *A*, Preoperative chest film. *B*, Operative thoracic ductogram demonstrating double duct throughout thorax. *C*, Film at discharge.

present. Urinalysis was not remarkable. Hemoglobin was 15.5 Gm.; red count, 4.7 million; hematocrit, 45; white count, 14,300, with a normal differential. Total protein was 4.5 Gm., 2.4 Gm. of albumin, 2.1 Gm. of globulin. A cervical node biopsy revealed malignant lymphoma of the lymphocytic type. Thoracenteses yielded 1,000 c.c. of typical chylous fluid from the right chest and a similar amount from the left. The patient was given a four-day course of intravenous nitrogen mustard therapy and discharged with no demonstrable benefit. She was readmitted on Dec. 22, 1952, because of increasing dyspnea. Physical findings were essentially unchanged on this admission. A chest film revealed increasing effusion bilaterally (Fig. 3, *A*). The total protein had declined somewhat, being 3.6 Gm. with albumin of 1.9 Gm. and a globulin of 1.7 Gm. As a palliative procedure, thoracic duct ligation was recommended and the patient had an exploratory operation performed on Dec. 27, 1952, through the bed of the right ninth rib. Upon opening the pleural cavity approximately 200 c.c. of chylous fluid was removed. The thoracic duct was identified above the diaphragm, transected, and both ends cannulated with polyethylene catheters. Methylene blue was injected proximally and distally in order to demonstrate the presence of a leak, but none was noted. Following this, 70 per cent Diodrast was similarly injected and a portable film obtained. The film demonstrated an accessory duct arising at the cisterna chyli with several cross connections with the cannulated duct (Fig. 3, *B*). This accessory duct was located, doubly ligated above and below, and the remaining duct was then ligated proximally and distally after the catheters had been removed. Following this, a decortication of the middle and lower lobes was carried out because of rather marked thickening of the visceral pleura. Postoperatively the patient had no farther effusion into the right chest, although persistent chylous effusion requiring thoracenteses occurred on the left side. The patient was treated by x-ray to the left pleura and mediastinum and intrapleural nitrogen mustard (Fig. 3, *C*). She was discharged April 19, 1953, and continued well until September when she gradually began losing ground and died on Nov. 22, 1953. Permission for post-mortem examination was not obtained. Following discharge until the time of death the patient remained free of dyspnea and required no additional thoracenteses.

Comment.—The surgical result in this instance was only partially successful. Chylous effusion, though controlled on the right, persisted, though to a lesser degree, on the left. This is construed as confirmatory evidence that chylothorax secondary to malignancy does not necessarily indicate rupture of the thoracic duct or a major radicle thereof, but probably results from extensive disseminated pleural "weeping" of chyle. The radiopaque injection of the duct at surgery resulted in excellent visualization and indicated another channel which was then located and ligated. Without this aid it is doubtful that this would have been accomplished.

CASE 2.—J. A., an 18-year-old white girl, was first admitted to the Albany Hospital on June 16, 1954, because of a painless swelling, of six months' duration, in the lower left aspect of the neck. On admission blood pressure was 130/70, pulse 100, respirations 20, temperature 98.6° F. Significant physical findings were limited to the neck where there was a nontender nodule palpable in the left lobe of the thyroid. A chest film was negative. Urinalysis and a complete blood count were within normal limits. On the day following admission the thyroid gland was explored at which time a cherry-sized nodule was noted in the left lobe of the thyroid and several suspicious cervical lymph nodes observed. A frozen section of one of the cervical nodes was reported as metastatic papillary adenocarcinoma in lymph node and accordingly a total thyroidectomy was performed. The patient's immediate postoperative course was uncomplicated and two days later, under general endotracheal anesthesia, a re-exploration was performed, with a left radical neck dissection and sternal split with lymph node dissection of the superior mediastinum.[12] During the procedure the left pleural cavity was entered, and the cervical thoracic duct was ligated and removed with the specimen. Catheters were placed in the left pleural space and superior mediastinum for drainage. The patient's postoperative course was uncomplicated and both

catheters were removed at the end of forty-eight hours. Fluoroscopy shortly prior to discharge on June 19 revealed excellent expansion of the left lung with no effusion in either pleural cavity.

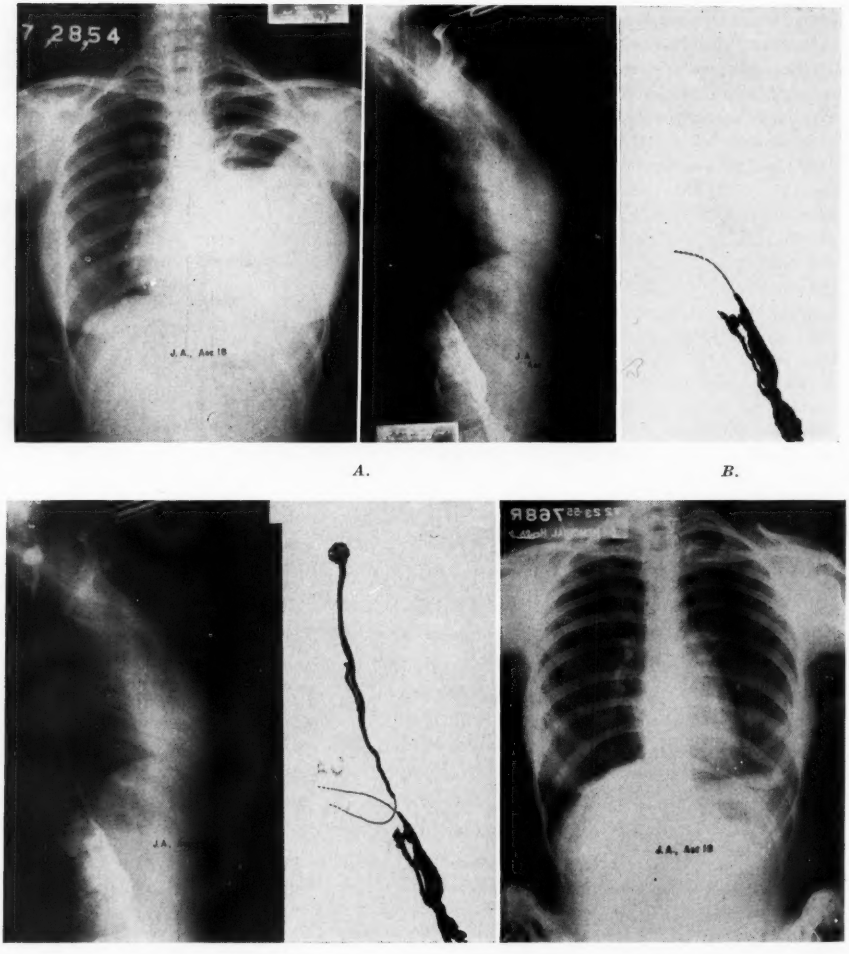


Fig. 4.—Case 2. Traumatic chylothorax in 18-year-old white girl following sternotomy and neck dissection for thyroid cancer. *A*, Left chylothorax on second admission seven weeks after initial operation. *B*, Operative injection of thoracic duct distally. *C*, After proximal and distal injection. There is a single duct at the diaphragm, a short double duct in midthorax. *D*, Chest film six months after ligation of thoracic duct at diaphragm.

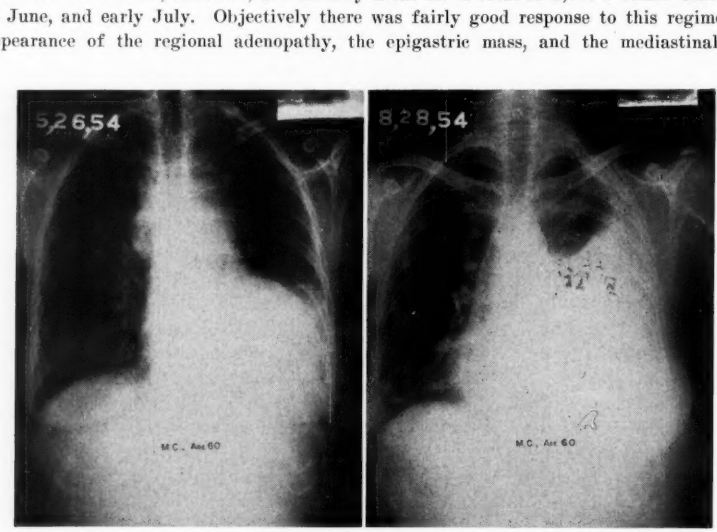
When she was seen two weeks following discharge there was noted, fluoroscopically, a small pleural effusion at the left base which was not considered significant. Three weeks later the patient complained of marked dyspnea and on fluoroscopy there was shift of the mediastinum and heart to the right with a massive left-sided pleural effusion (Fig. 4, *A*). Thoracentesis yielded 1,500 c.c. of chylous fluid which re-accumulated rapidly in a matter of four days and accordingly the patient was readmitted to the hospital on July 27, 1954.

Physical examination revealed the vital signs to be within normal limits. The cervical and sternotomy incisions were well healed and the left hemithorax was flat to percussion with diminished to absent breath sounds throughout. An intercostal catheter was inserted into the left pleural cavity and 1,200 c.c. of chyle obtained. The patient was then maintained on catheter drainage but during the ensuing thirteen days there was no abatement in the amount of drainage. Serum electrolytes at this time were within normal limits. Total protein was 6.3 Gm. with 3.9 Gm. of albumin and 2.4 Gm. of globulin. On Aug. 9, 1954, an exploratory operation was performed through the seventh left interspace at which time 1,600 c.c. of chyle were aspirated from the left hemithorax. There was no thickening of the visceral pleura, although there were adhesions between the upper lobe and superior mediastinal pleura. The aorta was mobilized just above the diaphragm by ligation and division of two pairs of intercostal arteries and retracted anteriorly with a Penrose drain. A somewhat enlarged thoracic duct was easily identified, and following division at this level both ends were cannulated with small plastic catheters. Several cubic centimeters of methylene blue were injected both proximally and distally into the thoracic duct through the catheters and extravasation occurred into the mediastinum at the apex of the thorax and somewhat to the left of the subclavian artery. No definite isolated area of leakage was noted but it appeared to be a diffuse process. Five cubic centimeters of 70 per cent Diodrast was injected into the distal catheter and an x-ray taken (Fig. 4, *B*), following which a similar amount of Diodrast was injected proximally and another x-ray obtained (Fig. 4, *C*). There was no evidence of a second thoracic duct and accordingly the catheters were withdrawn and the proximal and distal ends of the thoracic duct triply ligated with No. 2-0 silk. The pleural cavity was copiously irrigated with saline and the underlying lung re-expanded. The pleural space was drained with two separate catheters and routine closure of the wound carried out. Following this procedure the patient's postoperative course was uncomplicated and she was discharged on Aug. 17, 1954, on the eighth postoperative day. The patient has subsequently done well and at no time has there been any evidence of re-accumulation of chyle in the chest. A film obtained approximately six months following ligation of the thoracic duct reveals an essentially normal chest (Fig. 4, *D*). There is no evidence of further thyroid malignancy.

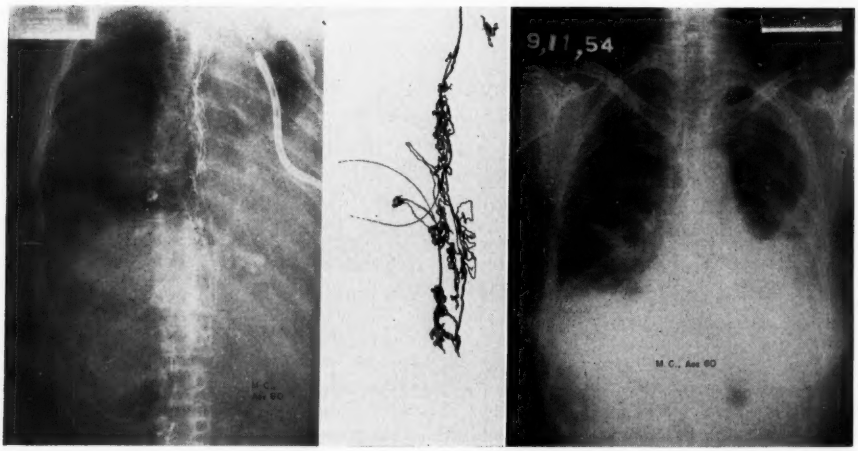
Comment.—Although the cervical thoracic duct was identified and ligated at the time of radical surgery on the neck, an unrecognized trunk was probably injured. That the chylothorax resulted from rupture secondary to ligation is highly unlikely in view of experimental evidence[4, 10] and in view of the findings at the time of low ligation of the duct. Demonstration of a single duct by contrast roentgenology at the time of ligation virtually assured a successful result. Approach to the duct from the left side in this case was greatly facilitated by anterior retraction of the aorta after division of two pairs of intercostal vessels.

Case 3.—M. C., a 60-year-old white single woman, was admitted to the Albany Hospital May 18, 1954, with a chief complaint of abdominal pressure, backache, malaise, and fatigue, of approximately three months' duration, associated with a 10 pound loss of weight. For two weeks prior to admission there had been increasing exertional dyspnea. Physical findings revealed a pale, chronically ill woman with obvious weight loss. Temperature 99° F., pulse 120, respirations 24, blood pressure 120/70. Supraclavicular and axillary adenopathy were noted. There was dullness with diminished breath sounds over the left chest posteriorly. The liver was palpable two fingers below the right costal margin and there was a large nontender mass in the epigastrium. Urinalysis was negative. A blood count revealed 11.2 Gm. of hemoglobin, with a red count, 3.6 million; hematocrit, 39; white count 5,400 with a mass and a left-sided pleural effusion (Fig. 5, *A*). A diagnosis of malignant lymphoma, normal differential. Films of the chest revealed the presence of a superior mediastinal

lymphoblastic type, was made by biopsy of a supraclavicular lymph node and the patient was treated with a four-day course of intravenous nitrogen mustard followed by x-ray therapy to the mediastinum, abdomen, and axillary areas for a total of 2,000 r tumor dose during May, June, and early July. Objectively there was fairly good response to this regimen with disappearance of the regional adenopathy, the epigastric mass, and the mediastinal tumor



A. *B.*



C. *D.*

Fig. 5.—Case 3. Chylothorax from lymphoma in 60-year-old woman. *A*, Chest film on admission showing mediastinal mass and left chylous effusion. *B*, Chest film three months later following x-ray therapy and two courses of nitrogen mustard. Mediastinal nodes have regressed but effusion has persisted and increased. *C*, Operative ductogram after injection. A second major duct is apparent by retrograde filling from the cisterna chyli. Both ducts shown connecting with midthoracic insula. *D*, Chest film nine days following interruption of duct. There is marked clearing but still persistent fluid with some air. Pleural reaction probably prevented full expansion of left lung.

on follow-up x-ray examination; however, the patient's complaint of dyspnea increased and it was necessary to perform thoracenteses with increasing frequency so that in the ensuing three months approximately 15 L. of chylous fluid had been aspirated from the left hemithorax. In August of 1954 the patient was again given a four-day course of nitrogen mustard therapy without appreciable benefit and because of a rather marked depression of the white count, additional x-ray therapy was not deemed advisable. Since, at this time, the patient's symptoms were exclusively related to her effusion, requiring thoracentesis once and frequently twice a week for relief, ligation of the thoracic duct as a palliative procedure was considered (Fig. 5, *B*). Following several transfusions to improve the patient's anemia she was taken to the operating room on Sept. 2, 1954, where, under general endotracheal anesthesia, left-sided intercostal catheter drainage was established with the immediate withdrawal of 1,500 c.c. of chylous fluid, the catheter then being attached to an underwater seal. The patient was then placed over a portable Bucky x-ray diaphragm, positioned in a supine position with slight elevation of the right chest and the table tilted 15 degrees to the left to elevate farther the right chest. A submammary incision was made from the axilla medially to expose the eighth interspace which was incised with transection of the costal arch. No fluid was encountered in the right hemithorax. The right lung was free of adhesions to the diaphragm or parietal pleura. Pulmonary ligament was partially transected and the right lung mobilized and retracted upward and out of the way. The diaphragm was retracted inferiorly and the mediastinal pleura entered just medial to the azygos vein. Tissues in this area were indurated and appeared to contain tumor in masses of nodes. It was feasible to identify a single large duct which was transected, catheterized distally and proximally with plastic catheters, following which 5 c.c. of 70 per cent Urokon was injected into the distally placed catheter and a film obtained, following which 10 c.c. was injected into the proximal catheter and an additional film taken (Fig. 5, *C*). The x-ray films indicated that the entire area above the diaphragm appeared to be composed of one accessory and numerous collateral ducts rather than the single duct which had been cannulated. Accordingly, after simple ligation of the major duct, transfixion sutures were placed just medial to the aorta through the anterior longitudinal ligament and tied. The area was packed with Oxycel gauze to promote fibrosis, following which the mediastinal pleura was sutured, the right lung re-expanded and a catheter left in the right chest. The patient's postoperative course was essentially uncomplicated and both catheters were removed by the third postoperative day. On the sixth postoperative day, a thoracentesis was performed on the left side and 500 c.c. of chyle was obtained. It was felt that this was residual and did not necessarily represent re-formation. At the time of discharge on the patient's ninth postoperative day she was ambulatory and afebrile; on x-ray examination the right chest was free of fluid and the left chest contained some fluid and incomplete expansion of the left lung (Fig. 5, *D*). Following discharge the patient did fairly well but gradually continued on a downhill course and was readmitted for terminal care, dying on Oct. 8, 1954. Although this patient survived surgery for only a period of slightly over five weeks, during that time she was clinically free of dyspnea and required no additional thoracenteses. Even on her final admission, breath sounds were clear bilaterally. At autopsy, generalized lymphoma involving the cervical, supraclavicular, axillary, inguinal, mediastinal, aortic, mesenteric, and hilar nodes was noted, as well as extensive involvement of the left parietal pleura and pelvic peritoneum. There was minimal fluid in the right chest and 300 c.c. of chyle in the left chest.

Comment.—Thoracic ductography at operation indicated that simple ligation of the cannulated duct would probably have been ineffective. It is felt that in this case the many collaterals resulted from the underlying disease. Though survival was brief following surgery a satisfactory result with regard to marked decrease in chylothorax was apparent, The right submammary approach was utilized since it was considered to be a more rapid and less traumatic

route in this debilitated patient. The extensive left-sided mediastinal and pleural involvement by tumor noted at autopsy would have made a left-sided approach to the duct impossible.

DISCUSSION

The surgical management of traumatic chylothorax is well established, and though all observers recommend early conservative management, recent reports[1, 16] indicate a more aggressive attitude favoring earlier surgical intervention when it becomes apparent that lesser measures are ineffective. In general, simple ligation of the duct at diaphragmatic level is definitive and the procedure of choice. Other technical methods including plastic repair of the duct as advocated by Seaman[17] or implantation of the duct into the azygos vein as proposed by Hodge and his associates[8] are based upon the repudiated premise that ligation will result in rupture of the duct, are technically more difficult and time consuming, and are certainly not applicable in all instances. We concur with those who favor exploration on the side of the chylothorax in traumatic cases, since complete evacuation of chyle from that hemithorax is possible and decortication can be accomplished if indicated. Traumatic chylothorax on the left subsequent to esophageal resection with left-sided esophagogastrostomy is probably an exception.

Though less frequently encountered, spontaneous chylothorax not the result of neoplasm is also amenable to surgical correction and presents essentially the same problems in management as do the traumatic cases. In chylous effusion secondary to malignancy, which is relatively frequent, little information can be gained from the literature. Meade and his associates[13] reported a case in which exploration was performed twice for spontaneous chylothorax and, though malignancy was suspected, it was not proved until later. Deliberate surgical intervention for chylothorax secondary to neoplasm is at best palliative, and should be undertaken only when all other modalities of therapy, which are frequently effective in controlling such chylous effusion, have been attempted. Our results in the surgical treatment of two such cases are not striking but do suggest further evaluation and trial in selected cases.

Operative visualization of the thoracic duct system by the technique described is relatively simple, adds little to the operative time, and is felt to be of value in assessing the presence or absence of other trunks which may then be located and ligated. Since such variations are present at diaphragmatic level in approximately 30 per cent of the instances, the information gained is of obvious importance. Where lesions such as cysts or hygromas of the thoracic duct are undiagnosed even at exploration the method can be of distinct diagnostic value, and its routine employment is recommended.

SUMMARY

1. Anatomic studies of the thoracic duct system in 30 subjects by means of contrast roentgenography are presented.

2. A simple method of visualizing the entire thoracic duct system at surgery is described and 3 cases of chylothorax in which such operative thoracic ductograms were obtained are reported.

3. The surgical management of chylothorax is discussed and intervention in selected cases due to malignancy as a palliative procedure is suggested.

4. Routine use of operative thoracic ductography is recommended in operations for chylothorax.

The authors wish to express their thanks and appreciation to Dr. Arthur W. Wright, Professor of Pathology, Albany Medical College, for permission to carry on the anatomic studies in his department, and also to Dr. John F. Roach, Professor of Radiology, Albany Medical College, for his technical assistance and cooperation in this project.

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DISCUSSION

DR. ELMER P. R. MAURER, Cincinnati, Ohio.—The amazing adequacy of the collateral circulation about the thoracic duct was impressed upon me in May, 1953, when I was asked to see a 37year-old white woman with fluid in the right chest.

(Slide) I think you can see the accumulation here. Thoracentesis yielded 1,000 c.c. of creamy odorless fluid which had the characteristics of chyle. This was alkalinized and treated with ether. This was before this method of treatment and after, giving the characteristic reduction in volume. The patient was treated with multiple thoracenteses and closed tube thoracostomy drainage for a period of three weeks with removal of approximately 7.5 L. of chylous fluid without any improvement.

(Slide) On June 15, 1953, a right thoracotomy was performed through the eighth rib bed. You can see a cylinder-shaped tumor mass involving the thoracic duct, measuring approximately 2 cm. in diameter, situated between the azygos vein and the aorta. Chyle leaked constantly through pin-point openings in this tumor. As the dissection was continued it was found that the tumor involved the entire thoracic duct from the aortic hiatus up to the point where it crossed the midline into the opposite side and the thoracic inlet. The duct in the normal portion high underneath the left pleura was ligated and again inferiorly above the aortic hiatus, following which the entire tumor and thoracic duct were removed.

(Slide) Microscopically, the tumor resembled the characteristic picture of benign lymphangioma with numerous networks of irregular endothelium-lined channels containing lymph.

(Slide) The patient did well postoperatively and was ready to go home on the eleventh day. There was no recurrence of the chyle and, up to the present time, approximately two years after operation, she has done well.

To my knowledge this is the first case of primary benign tumor of the thoracic duct that has been reported in association with spontaneous chylothorax. Also, in a review of the literature I have encountered no instance of excision of extensive portions of the thoracic duct for any cause whatsoever. Obviously, as demonstrated as early as 1922 by Ferdinand C. Lee, the thoracic duct can be ligated with impunity and, following ligation (and I think this is important) collateral lymph circulation is established through embryonic lymph channels which normally do not function, which in response to ligation may be forced to enlarge and dilate. Also, following ligation lymphatico-venous connections are found to exist between the thoracic duct, the azygos, intercostal, and lumbar veins. The embryonic thoracic ducts are bilateral, symmetrical, and have numerous cross anastomoses. Despite the excellent demonstration Dr. Stranahan and his associates have presented today, I think the factor of excellent collateral circulation, particularly in light of the clinical experience I have just reported, would indicate that extensive resection of the thoracic duct is possible even in those patients who have a single canal, as reputedly occurs in some 60 per cent of the cases.

DR. ROY KLEPSER, Washington, D. C.—It is surprising how many surgeons operating in the neck, mediastinum, and upper abdomen, within a few centimeters of the thoracic duct, have never taken the trouble to expose it and to look at it, much less to wonder what they would do if they did cut it.

In 1949, while discussing the paper of Dr. Meade at the New Orleans meeting, I presented a method of diagnosis of chylothorax with the aid of lipophilic dyes. My purpose in devising the test was to outline the thoracic duct for verification at the time of operation. This did not work well as the dye was not concentrated enough. It was a rather pastel color in the duct, and the duct did not visualize because of the pale color in the rather opaque duct. However, the fat in which the dye was fed to the patient distended the duct, making it easily identifiable. If one gives the patient a small amount of olive oil or butter preoperatively, the duct can be seen to be the size of a lead pencil instead of the size of the lead of a pencil. We are used to seeing the duct in a collapsed state in the cadaver, or in the starved state in which we operate on patients, so we seldom see a distended duct. The duct thus becomes much more readily identified if it is distended with oil preoperatively.

In using the dyes diagnostically the dye is mixed with butter and is fed to the patient the night before thoracentesis. It is better to feed it as a sandwich, in the dark, because the dyed butter looks like used wagon grease. It is spread thickly, about a quarter pound of butter with an ounce of the dye. The following day the chest is tapped. The chyle, which has been milky or possibly blood-tinged, will then be green, or purple, or red, depending on the dye used. This test not only tells us that it is chyle, but also tells us that the duct is still leaking.

Our method of ligation is to go in on the right side through an anterolateral incision between the ribs, ligating the duct above the diaphragm. I have ligated twenty-seven thoracic ducts in the past five years. Nine ligations were for ruptured thoracic ducts. The other

eighteen ligations were in unresectable carcinoma cases, the ducts being ligated while the chest was open in order to evaluate the effect of its ligation. In no cases were there harmful effects from this.

DR. LYMAN A. BREWER, III, Los Angeles, Calif.—I think the essayists have presented a real contribution because the location of the duct and its tributaries is sometimes most important. We have recently reviewed a series of 24 cases of thoracic duct lesions of various types. This report will be published in the *American Journal of Surgery* in the near future. In the cases studied in our series, the most common source of leakage of chyle from disease is not in the thorax, but in the abdomen. Therefore the failure of treatment of chylothorax by ligation of the duct or other procedure may be explained by the fact that the chyle is extravasated below the diaphragm and leaks up into the chest along the paravertebral space to seep out into the mediastinal pleura to the thorax. The chyle may also extravasate down the leg or up into the cervical region or even out into the arms. Therefore no exploration is complete without a search for the pathology in the abdomen or retroperitoneal tissues. We believe that it is important that the surgeon recognize the wide collateral circulation of the thoracic duct system, for this permits ligation of the thoracic duct in the neck and in the thorax and, in most instances, in the upper abdomen above the cisterna chyli. The lesions below this level, which are primarily obstructive in nature, present a more complex problem.

We have recently reported a case of a neurogenic tumor involving the thoracic duct at the cisterna chyli. In this case the subdiaphragmatic collection of chyle worked its way along the paravertebral space and through the various diaphragmatic hiati and into the pleural cavity. This was discovered for the first time when the thorax was explored to determine the cause of a persistent spontaneous chylothorax. When the chyle was obviously coming up from below the diaphragm, this structure was opened to reveal the true source of the disease. After excising the neurogenic tumor which had caused the obstruction of the afferent ducts to the cisterna chyli, we found that there was a dilatation of one of the major ducts which, after ligation, was on the point of rupturing. It was obvious that decompression of this duct was necessary, for we had merely reproduced the obstructive phenomena of the tumor. Therefore a side-to-side anastomosis of the thoracic duct to the hemi-azygos vein was successfully completed. There has been no recurrence of the chylothorax or drainage of chyle below the diaphragm for over three years, pointing to the fact that the anastomosis must still be patent. We believe the principle of decompression of the thoracic duct, which has ruptured as the result of obstruction, is sound. It probably has application only in the abdominal portion of the duct and, from the clinical and experimental evidence at hand, most often in the afferent branches to the cisterna chyli. Since the abdominal lesions were most common in the series that we have studied, further application of this technique will be indicated. The manner of identification of the branches of the thoracic duct presented by the authors is of considerable importance, for it may make possible the performance of thoracic duct venous anastomoses in certain cases.

DR. W. O. MILLS, Seattle, Wash.—I have enjoyed this presentation very much, and the beautiful contrast medium studies presented are certainly helpful in visualizing the often plexiform nature of the thoracic duct channels. However, I think we ought to remember that our success in ligating such a complex structure may not be as high as we think at the time we see the operation. We should also remember that despite the quality of our visualization and the delicacy of our dissection, one of the things that controls chylothorax is obliterative pleuritis. In each of the cases presented today, whether the chylothorax is bilateral or unilateral, the benefit from the operation lies on the side that was operated upon. In each instance the costophrenic angle was flattened and there is evidence of obliterative pleuritis on the operated side. It may be that this has contributed to the good control of the chylothorax. As far back as 1943, I remember a right chylothorax due to a gunshot wound that was treated by aspiration of the chyle and intrapleural injections of glucose solution. We got a very prompt and good result. I believe that often the obliterative pleuritis is the thing that controls the situation.

DR. KAUSEL (Closing).—My associates and I would like to thank the discussants for their remarks. With regard to Dr. Maurer's comments, I think other cases of hygromas or lymphangiomas of the thoracic duct have been reported; Dr. Brewer's case certainly sounds like one and I think Drs. Touroff and Seley reported such an instance. We are well aware of Dr. Klepser's work with lipophilic dyes and we concur that they are of great diagnostic value. We did not discuss diagnosis in this paper.

Dr. Brewer's remarks about associated chylous ascites are quite true. We have seen such a case of chylous ascites associated with chylothorax. We did not operate on this patient, the ascites and effusion being controlled by other means. With regard to Dr. Mills' discussion, I believe his observations about the efficacy of the obliterative pleuritis are quite true; for these reasons I think that in traumatic cases the approach should be through the side of the chylous effusion. At this time the chest can be completely exacuated of chyle and if necessary, and not infrequently it is, the lung can be decorticated. This then lends itself to a good pleuritis. However, I have one reservation; that is, in those cases with apparently adequate tube drainage, where the leak persists for two or three weeks and, following ligation of the duct, stops, obliterative pleuritis is not the entire answer—I do not know the entire answer to it, and I think it is imporant.

We would like to make one other comment, with regard to intervention in cases of malignancy. We do not recommend this as a routine measure and the majority of the cases we have seen have responded to intravenous nitrogen mustard and x-ray, or intrapleural nitrogen mustard, and obviously those modalities should be tried first in cases secondary to malignancy.

DR. EDWARD S. WELLES, Saranac Lake, N. Y.—I have been very quiet throughout this entire meeting, but at this time I want to compliment those who discussed this paper. All the discussions have been pertinent to the subject and have dealt with the thoracic duct. I should like to call to the attention of the younger men particularly the fact that this is the type of discussion we ought to have. So many young men look over a program and find a subject that has some vague connection with what they want to say, so they take the opportunity to appear on the platform with a lot of statistics and present what is really a paper, although it would not be accepted as such, which has merely some faint relationship to the subject at hand. Therefore, I want to go on record as complimenting all the men who discussed this paper.

Editor's Note

It is to be regretted that the next paper by Dr. Charles B. Ripstein of New York, entitled "Complications of Mitral Valve Surgery With Particular Reference to the Post Commissurotomy Syndrome," was not turned in for publication. Efforts to obtain the paper were unsuccessful. Under the circumstances it seemed of no value to publish the interesting discussions of it which were given by Dr. Charles P. Bailey, Dr. Harris B. Shumacker, Dr. Egbert H. Fell, and Dr. E. D. Cagnon.

EVARTS A. GRAHAM.

VASCULAR CHANGES IN BRONCHOPULMONARY SEQUESTRATION

Observations in Two Cases With Multiple Accessory Systemic Arteries

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THE occurrence of aberrant systemic arteries to the lung has been noted with increasing frequency and interest since the advent of modern thoracic surgery. While earlier reports[1-4] dealt primarily with cases encountered in the anatomy and pathology laboratories, the more recent publications have stressed the frequency and importance of this syndrome in surgical diagnosis and treatment. Several excellent recent reviews of this subject[5-11] obviate the necessity of our reiterating the existing literature at this time. Instead, we propose to summarize briefly certain aspects of the current knowledge in this field and to add to it certain observations based on detailed personal study of two cases of multiple accessory systemic arteries to the lung.

Most aberrant vessels to the lungs originate from the descending aorta, usually just above the diaphragm or sometimes just below it. While the occurrence of aberrant vessels with origins from other large systemic arteries has been reported, such arteries are more likely to be associated with anomalies of the cardiovascular system. In all the cases of accessory systemic arteries arising from the lower thoracic aorta which have been reported to date, only one aberrant artery was found to course to any one lung. Where two such vessels have heretofore been found, they entered opposite lungs. Aberrant systemic arteries may supply a lung which is otherwise entirely normal; but the majority of such vessels have been distributed to areas of the lung, most commonly the lower lobes, which also showed other abnormalities. In most cases the affected lobe or some of its segments have been the seat of multiple cysts or of marked cystic bronchiectasis. Frequently, the dilated bronchi cannot be demonstrated to have significant communications with the remainder of the bronchial tree (intralobar sequestration). Accessory systemic vessels have at times been found in association with anomalies of the diaphragm. There is general agreement that accessory systemic arteries to the lung as well as the associated pulmonary abnormalities are congenital in origin. The exact mode of origin of these changes is in doubt. Of the various theories which have been proposed to account for this syndrome,[5, 6, 8-10, 12] Pryce's views have found wide acceptance in recent years.

The structure of the aberrant vessels was also studied by Pryce.[5] He found them to be elastic arteries and in comparing them to pulmonary arteries noted that the former were thicker walled and contained more elastic tissue.

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While commenting on these quantitative differences between the two types of vessels, he apparently found no qualitative differences in their structure. He concluded that the aberrant vessels were indeed pulmonary in origin. Pryce also observed varying degrees of atheromatosis in aberrant systemic arteries and also called attention to Batts's[4] previous description of degenerative changes in such anomalous vessels. Bruwer and associates[8] also observed such degenerative phenomena and regarded them as possibly related to the patient's age and to sepsis as well as to the fact that the portion of the lung supplied by the aberrant artery is usually nonfunctioning. These authors also subscribed to Pryce's view that these vessels differ only quantitatively from pulmonary arteries. In none of these studies was there any attempt to relate the degenerative changes in the aberrant vessels to the presence or absence of such changes in the normal pulmonary vessels.

Clinically, accessory systemic arteries by themselves do not give rise to symptoms or signs. The associated pulmonary changes may be symptomatic when secondarily infected. This, as well as their discovery on survey chest roentgenograms, usually brings them to the surgeon's attention. The necessity for awareness of the occurrence of aberrant systemic arteries, especially in the performance of pulmonary resections in young individuals with cystic lesions, was emphasized by Douglass[7] and Harris and Lewis.[13] Death from exsanguination when such a vessel was inadvertently injured in the course of lobectomy has been reported.[13]

The coexistence of pulmonary abnormalities and pulmonary tumors, especially the so-called bronchial adenomas, has been repeatedly noted and emphasized by Womack and Graham.[14, 15] Until now, no tumors have been reported in lobes with bronchopulmonary sequestration and aberrant systemic arteries.

CASE REPORTS

CASE 1.—(R. F., No. 53740.) The patient was a 14-year-old white boy who was admitted to the Jewish Hospital of St. Louis on April 10, 1953, with the history that he was in apparent good health until approximately four months previously when he had "flu" which was associated with chills, fever, cough, and expectoration. Under treatment by his local physician his symptoms improved rapidly. About one month later, he began to have a mild cough, productive of approximately one teaspoonful of pinkish sputum daily. On April 3, 1953, a routine survey chest roentgenogram taken at school showed a lesion in the left lower lobe and the patient was advised to consult his physician. A tuberculin patch test had been negative in January, 1953. During these months, the patient continued to feel well and took part in competitive high school sports. His past history was relevant only in that he had had mild asthma since early childhood. The last attack had occurred seven months prior to admission. Six years previously he had had pneumonia from which he made an uneventful recovery.

Physical examination on admission showed a well-developed, well-nourished 14-year-old boy who was not acutely ill. Examination of the chest revealed normal expansion. Percussion note was resonant. Breath sounds were within normal limits and there were no râles. The remainder of the physical examination was similarly unrevealing.

All laboratory studies, including urinalysis, blood counts, Kahn test, serum protein, blood sugar, and urea determinations were within normal limits. Sputa were negative for acid-fast bacilli. Tuberculin and histoplasmin skin tests were negative. Roentgenogram of the chest showed a cavitary lesion in the posterior basal segment of the left lower lobe in which

a fluid level was seen. Bronchoscopy on April 13, 1953, showed a small amount of purulent material coming from the left lower lobe orifice but there was no tumor or other obstruction.

A tentative diagnosis of pulmonary cyst or chronic lung abscess was made and the patient was scheduled for operation and meanwhile discharged from the hospital on sulfadiazine, 1 Gm., four times daily. He was readmitted to the hospital on April 26, 1953, with no complaints. He had been asymptomatic since his discharge. Physical examination and laboratory studies were again unrevealing. A new chest roentgenogram showed no change in the appearance of the lesion.

On April 30, 1953, left lower lobectomy was performed under endotracheal ether anesthesia. At operation a cystic lesion was found in the posterior basal segment of the left lower lobe. In palpation of the inferior pulmonary ligament, pulsating vessels were felt. By careful dissection, six arteries varying in diameter from 2 to 5 mm. were successively identified and divided after ligation. Each of these vessels originated in the descending aorta about 3 to 4 cm. above the diaphragm and entered the left lower lobe below the inferior pulmonary vein through the pulmonary ligament. The remainder of the lobectomy was accomplished in routine fashion.

The patient's postoperative recovery was uneventful and he was discharged from the hospital on May 10, 1953. He has remained well since then.

Fig. 1.—Gross specimen, Case 1. A portion of the diseased lung has been bisected showing numerous small unilocular and larger multilocular cysts.

Gross Pathologic Description.—The specimen consisted of the lower lobe of the left lung. In the lobar hilum, the artery and bronchus to the basal segments as well as the separately divided apical segment artery and bronchus were identified. At the medial and posterior aspect of the lobe below the inferior pulmonary vein, six ligated arteries could be seen. They varied in size from 1 to 3 mm. in diameter and were relatively thick walled. Over the posterior basal segment, the visceral pleura showed numerous old fibrous adhesions. This area of the lobe felt firm and indurated. The abnormal part of the lobe was sharply demarcated. Under fluoroscopy Diodrast was injected into the basal segment artery of the lobe. This artery was seen to divide into two segmental branches which supplied the anterior and middle basal segments. The posterior basal segment did not receive a grossly recognizable branch and scarcely showed opacification by the dye. Injection of anomalous arteries with Diodrast was then done and resulted in visualization of a branching network of vessels. The

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posterior basal segment became opacified after this injection. Dissection of the bronchial tree showed two major segmental bronchi arising from the common basal segmental bronchus. These bronchi and the apical segmental bronchus skirted the indurated posterior basal segment but did not supply it except for one small branch about 2 mm. in diameter which entered this segment. On further sectioning of the lobe, the entire lobe with the exception of the posterior basal segment was found to be normal. The posterior basal segment was entirely replaced by one large cyst measuring about 5 cm. in diameter and numerous smaller cysts which varied in size from less than 1 mm. to 1.5 cm. in diameter. The previously mentioned small bronchial branch was the only recognizable communication between the large cyst and the remainder of the bronchial tree. The intervening pulmonary parenchyma was firm, grayish, and speckled with small yellowish and brownish areas (Fig. 1).

Microscopic Description.—Sections were taken from the uninvolved portion of the lobe, through the anomalous arteries and from various portions of the abnormal segment of the lobe and were stained with hematoxylin and eosin, and Verhoeff's elastic tissue stain. In addition, micro-incinerated sections were examined with the dark field technique. Sections through the posterior basal segment showed the normal architecture of the lung completely destroyed. Instead there were innumerable small cystlike spaces as well as larger cysts.

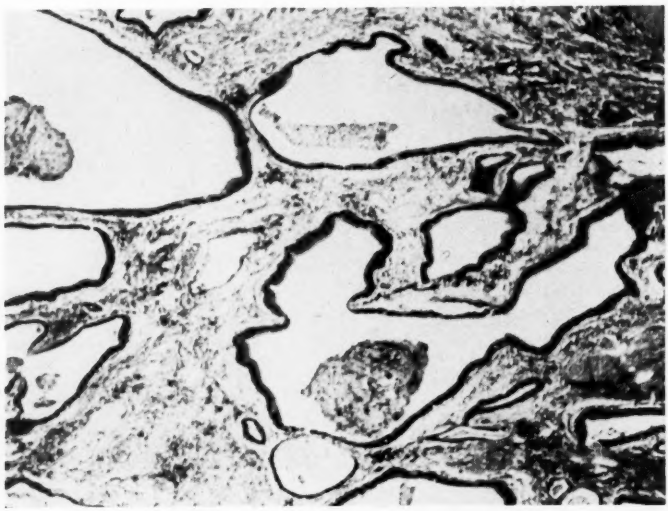

Fig. 2.—Photomicrograph of a section through a cystic portion of lung in Case 1 and showing numerous cystic structures variously lined by cuboidal, columnar, and ciliated columnar epithelium. Interstitial stroma is of loose connective tissue, and some cysts contain inspissated secretion. (Hematoxylin and eosin stain, ×200.)

The larger cysts were lined by tall columnar ciliated epithelium. The smaller cysts showed a lining which was sometimes cuboidal, ciliated, and obviously secretory, at other times low cuboidal and nonciliated. Many of the smallest cysts were partly lined by one type of epithelium and partly by another (Fig. 2). The lumen of the cysts contained mucoid material which was lightly pink staining with hematoxylin and eosin, and mononuclear and multinucleated phagocytic cells. There were also a few lymphocytes, but no appreciable number of polymorphonuclear leukocytes. Beneath the epithelium of the largest cyst there were scattered groups of smooth muscle fibers and small rounded pieces of cartilage. A few mucus glands were also present in the wall of this cyst. The intervening tissue

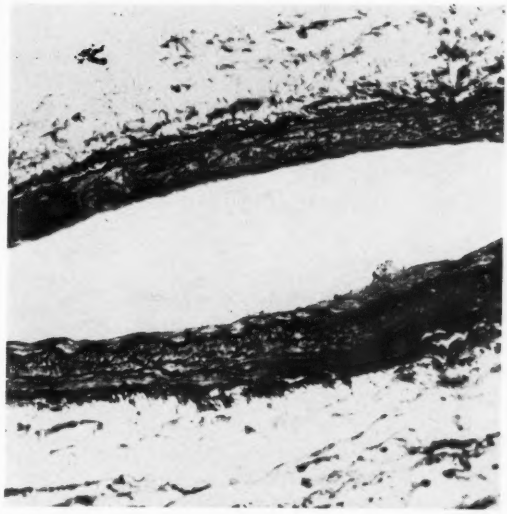

Fig. 3.—Photomicrograph of a section through a third order pulmonary arterial branch in Case 1. Note early intimal thickening in lower right-hand corner. (Verhoeff's elastic tissue stain, ×200.)

Fig. 4.—Photomicrograph of a section through a primary artery to left lower lobe in Case 1. Note diffuse elastosis of intimal elastic plaque. (Verhoeff's elastic tissue stain, ×200.)

between the cysts consisted of connective tissue, histiocytes, and lymphocytes which frequently occurred as definite lymph follicles. Sections from other portions of the lobe showed normal lung tissue, except for the vessels. The large pulmonary arteries supplying uninvolved portions of the lobe showed early intimal plaque formation. These consisted of small subintimal accumulations of connective tissue and numerous small elastic fibers (Figs. 3 and 4). The arterial wall showed the usual number of relatively short fairly thick elastic fibers. In the incinerated preparations, such vessels showed increased mineral content in the wall. There was an accentuation of mineral deposition in the intima in some pulmonary arteries. Smaller arteries and arterioles in the uninvolved parts of the lung showed no deviations from normal and the venous system was also not remarkable. In one section a small bronchial artery in the wall of a rather large bronchus showed mild diffuse intimal proliferation.

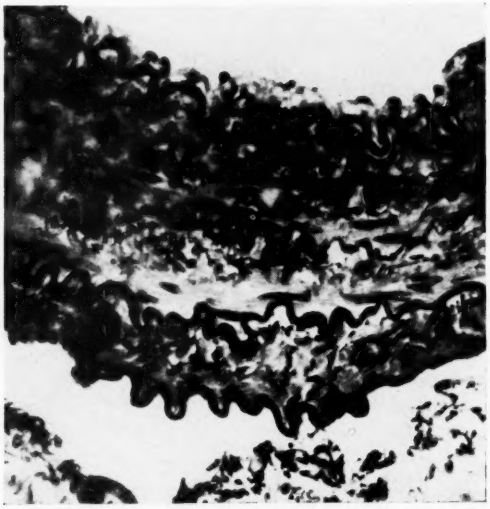

Fig. 5.—Photomicrograph of a section through a systemic artery in Case 2. This is characteristic of artery of hybrid type. Note greater proportion of muscle than in Figs. 4 and 8 and thicker, longer elastic fibers. (Verhoeff's elastic tissue stain, ×450.)

Sections through the systemic arteries showed them to have a different appearance from pulmonary arteries. These vessels were relatively much thicker walled than pulmonary arteries. Their media consisted of concentric lamellas of long undulating elastic fibers. In brief, these vessels had the appearance of hybrid arteries such as the visceral branches of the abdominal aorta (Fig. 5). They showed no evidence of intimal thickening or plaque formation and in incinerated preparations no increased mineral content could be seen (Fig. 6). In the posterior basal segment of the lobe numerous large arteries with the appearance of pulmonary arteries were found. Some of these large vessels were present even at the periphery of the segment in intimate association with the largest cyst. In many of these large pulmonary arteries very marked intimal thickening and plaque formation had occurred. In the micro-incinerated sections these vessels showed a considerably greater mineral content than comparably sized pulmonary arteries from uninvolved parts of the lobe (Fig. 7). Some of the sections showed in addition small branches of the aberrant vessels. These were readily identified by virtue of their different histologic structure and here, too, they showed no degenerative changes. Examination of the smaller, predominantly muscular branches of the pulmonary arteries showed changes in them which were as pronounced as those described in the larger arteries. There was extensive intimal thickening and some graying and splitting of the internal elastic lamella.

Fig. 6.—Photomicrograph of a micro-incinerated specimen. Section through a major aberrant artery. Mineral ash is considerably less than in Fig. 7. White streaks represent nuclei of muscle cells of media. (×450.)

Fig. 7.—Photomicrograph of micro-incinerated section through a third order pulmonary artery branch in Case 1. Note white mineral ash (calcium) diffusely spread through the media. A thin line of calcium at top of specimen represents endothelium, and clear area immediately underneath represents subendothelial fibrous thickening. (×450.)

On micro-incineration some increased mineral content of the intima was again seen. These changes were not isolated and scattered, but rather involved the majority of the smaller vessels in all sections from the affected segment. The small and larger veins of this segment showed a very extensive phlebosclerosis. This consisted of marked intimal thickening and plaque formation and increased mineral content of the intima. The venous system in the uninvolved lung segments was normal.

In summary, the vascular findings consisted of isolated plaques in the large pulmonary arteries supplying normal segments of the lobe, and marked plaque formation and intimal thickening in the large pulmonary arteries in the affected segment. The smaller arteries in this segment almost universally showed marked intimal proliferation and the veins showed moderately advanced phlebosclerosis. The aberrant arteries were readily distinguished from the pulmonary arteries by virtue of their appearance either as that of a miniature aorta or a hybrid artery. They showed no degenerative changes.

Case 2.—(R. D. L. No. 3739.) A 60-year-old white man was admitted to the Jewish Hospital on June 1, 1937, with the history that in September, 1936, he had noted a raw area on the left buccal mucosa. He was operated on elsewhere in October, 1936, for a carcinoma of the cheek with excision of the ulcer and "parts of bone." Because of recurrence of the lesion, he returned to his local hospital for a second operation in December, 1936, and two weeks later, in January, 1937, the patient again noted a recurrent ulcer. For two to three days prior to his admission to the Jewish Hospital he had been unable to eat solids. He had no pain and there was no marked weight loss. He had chewed tobacco for many years. He had no respiratory symptoms. Physical examination on admission showed a man who was not acutely ill. There was a large clean ulcer in the left cheek with induration extending toward the nose and induration and swelling of the upper lip almost to the left commissure. There was a large ulcerated area on the buccal mucosa. The patient was able to open his mouth only with great difficulty and then only to a very slight degree. There were several enlarged firm, left anterior cervical nodes. The chest was emphysematous. Breath sounds were within normal limits. There were no râles. The remainder of the examination was within normal limits. On June 3, 1937, under general anesthesia, a radical dissection of the face and neck was carried out. On June 8, 1937, the patient suddenly became markedly dyspneic and died. An autopsy was performed.

Gross Pathological Description of Lungs.—The pleural cavities were largely obliterated by dense fibrous adhesions. These were particularly tenacious in the area between the base of the left lung and the left hemidiaphragm. The right lower lobe showed a small area of consolidation but there were no abscesses or cavitations. In the left lower lobe a large irregular cavity lined by smooth brownish tissue was found. A series of cartilage plates were found in one portion of the wall of this cavity and there were also numerous pockets and recesses. However, no connection between the cavity and the bronchial tree could be demonstrated. In the removal of this lobe, two arteries which had the appearance of large intercostal arteries were encountered. They originated about 5 cm. above the diaphragm from the thoracic aorta and entered the posteromedial aspect of the left lower lobe. They communicated with a large artery which coursed along the posterior aspect of the cavity.

Microscopic Description.—For this study there were available blocks of tissue from the right lung and blocks from various portions of the left lower lobe. There were no blocks through the anomalous systemic arteries. Hematoxylin and eosin stains, Verhoeff elastic tissue stains, and micro-incinerated slides were studied. The sections from the right lower lobe showed the normal pulmonary architecture to be well preserved. There were patchy and confluent areas of bronchopneumonia but no other abnormalities. Sections from the left lower lobe showed only scattered areas in which the normal alveolar structure of the lung was recognizable. The grossly observed cyst consisted of an inner lining of cuboidal ciliated epithelium. This was surrounded by connective tissue in which smooth muscle bundles occurred. Irregular cartilage plates were present in the cyst wall and there

were many bronchial mucus glands. The surviving pulmonary alveoli and small bronchioles and bronchi in the remainder of the lobe showed infiltration with lymphocytes, polymorphonuclear leukocytes, and macrophages. Intervening between these persisting islands of lung tissue was a dense connective tissue stroma in which other scattered pulmonary structures could be found. There were small cystic structures lined by cuboidal epithelium, irregular cartilage masses unassociated with bronchial structures, and masses of lymphoid and fatty tissue. In several sections from the wall of the large cyst, one could see masses of a tumor which was composed of small deeply staining rather regular cells with relatively large nuclei. These nuclei, while relatively homogeneous, did show some variation in appearance. Some were pyknotic and deeply staining, while others were rather vesicular. Mitotic figures were rare. The cells were arranged in small masses which had a pseudoacinar or alveolar appearance. These cell masses were separated from each other by delicate connective tissue septa. The tumor was invasive but had not ulcerated or invaded the overlying epithelium of the cyst.

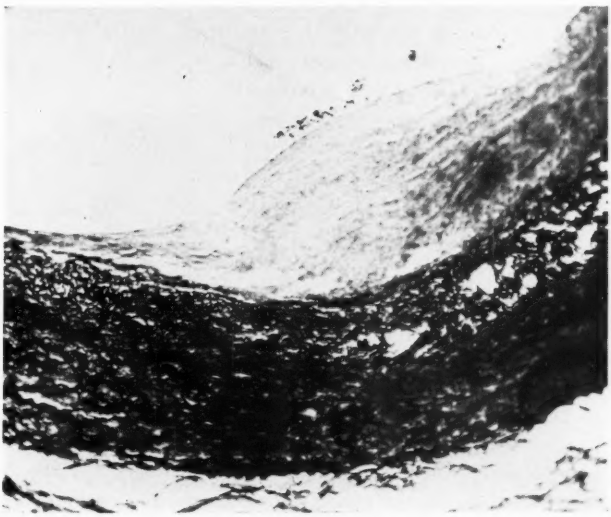

Fig. 8.—Photomicrograph of a section through primary artery to left lobe of Case 2. Note thick hyaline intimal plaque and dense elastosis of media beneath plaque. (Verhoeff's elastic tissue stain, ×200.)

Study of the vasculature of the lungs resulted in the following observations. In the right lower lobe, the vessels were not unusual. Mild to moderate degrees of arteriosclerosis of the pulmonary arteries was present and consisted of intimal thickening and formation of scattered small plaques. The internal elastic membrane of many arteries was split or frayed. The veins were normal. In the left lower lobe, large pulmonary arteries occurred far out at the periphery of the lobe. They were in close association with the cyst. Their histologic appearance was characteristic of pulmonary arteries and they were the seat of a most advanced arteriosclerosis. Large subintimal connective tissue deposits and huge plaques of hyalinized connective tissue were common (Fig. 8). In many of these arteries the lumen was decreased by as much as one fourth to one third. The internal elastic lamella was thick, split, and hyalinized. In micro-incinerated sections these arteries showed a very marked increase in mineral ash content throughout their wall. Smaller arteries in the left lower lobe also showed marked degenerative changes. Intimal thicken-

ing and increased mineral content of the intima were again observed. At the same time these sections revealed an unusually intense phlebosclerosis. In some instances, this almost rivaled the severity of the arterial changes.

COMMENTS

These 2 cases emphasize several points which have not previously been reported. Perhaps one of the most important to the practicing surgeon is the presence of multiple aberrant systemic arteries in both of these cases, six in Case 1 and two in Case 2. From the surgical viewpoint, this means that every caution must be exercised in the dissection of such lobes even after one aberrant artery has been found and safely divided. The occurrence of a bronchial adenoma of the oncocyte-carcinoid type in the wall of the cyst of Case 2 is of equal importance. The malignant potentialities of these tumors are generally recognized today. Their not infrequent coexistence with congenital abnormalities of the lung is not so widely appreciated, but this is one of the important indications for surgical intervention for apparently benign cystic lesions even in the absence of clinical symptoms.

From our observations it would appear that, contrary to the view expressed by Pryce and others, the aberrant arteries are not pulmonary in type. Unfortunately, our second case was autopsied 15 years ago and we did not have sections through the arteries themselves available to us. However, in Case 1 these arteries differed strikingly from pulmonary arteries. The walls of aberrant vessels are thicker and the media contains long, plump elastic fibers arranged in concentric lamellas. These vessels also contain proportionately more muscle tissue than the pulmonary arteries. In the latter the elastic fibers are short and irregular, and the arteries are relatively thin walled. The aberrant vessels thus resemble systemic elastic or hybrid arteries. They are built to withstand high pressures. In Case 1, the aberrant vessels showed no degenerative stigmas. By comparison, the arteries and the veins in the affected lung segment showed advanced sclerosis and even the larger pulmonary arteries supplying uninvolved segments showed early arteriosclerosis to a degree which one would not expect in so young a subject in the absence of pulmonary hypertension. Even in the older man in Case 2, the arteries and veins of the left lower lobe showed changes much more severe than one would expect solely on the basis of age and too such changes were absent in the vessels of the normal right lung. These changes in the pulmonary arteries are similar to those described by Gray and co-workers[16] in pulmonary hypertension due to mitral stenosis and other causes. Pareira and associates[17] have shown that elevation of pressure plays an important role in the development of arteriosclerotic lesions. This is particularly true in the case of pulmonary vessels which are not constructed to withstand the higher systemic blood pressure. These facts point to the presence of a systemic-pulmonary shunt.

As one would expect, the pulmonary vessels in the immediate vicinity of the aberrant systemic vessels sustain the greatest damage due to increased pressure. However, this hypertension is apparently reflected, although to a

lesser degree, in all parts of the pulmonary circulation. The advanced phlebosclerosis is probably related to the presence of communications between the aberrant arteries and the pulmonary venous system. The presence of such communications is suggested by the injection studies of Lemmon and associates[18] and also by our own study of a recent case of bronchopulmonary sequestration. In this case injection of the aberrant artery with Lipiodol, a material which because of its viscosity would hardly be expected to fill rapidly vessels of capillary size, resulted in almost immediate visualization of the pulmonary vein (Fig. 9). Taking into consideration the structure of the aberrant arteries, it is not surprising that they show the least evidence of degenerative change. It seems logical to assume, however, that with progressive pulmonary arteriosclerosis and phlebosclerosis, the pressure in the aberrant artery would eventually increase so that it, too, would finally show arteriosclerotic stigmas. Previous authors noted the occurrence of such changes in aberrant arteries, but they failed to study the degree to which the pulmonary vessels shared in this process. We believe that their cases represent the end result of a process of which our Case 1 presents an early stage.

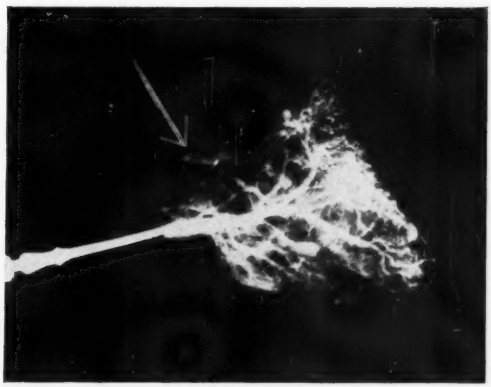

Fig. 9.—Radiograph of a left lower lobe with bronchopulmonary sequestration after injection of aberrant artery with Lipiodol. Cannula is in artery. Arrow points to pulmonary vein.

SUMMARY AND CONCLUSIONS

Two cases of congenital cystic malformation of the lung with multiple aberrant systemic arteries are presented. The importance of guarding against injury to these vessels in the course of lobectomy has been emphasized. In particular, one must continue to be on the lookout for further aberrant vessels if one such artery has been found. In one of our cases, a bronchial adenoma was superimposed on the congenital abnormality, thus underscoring once more the need for removal of all undiagnosed lesions of the lung.

Histologic study of the intra- and extrapulmonary portions of the aberrant arteries suggests strongly that they are systemic in origin. It was found that the aberrant systemic arteries bring about arteriosclerotic changes in the

pulmonary vasculature, both arterial and venous, as the result of hypertension in the lesser circulation due to the presence of a systemic-pulmonary shunt. Arteriosclerosis of the aberrant systemic arteries themselves appears to be a late manifestation of this condition.

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PLASMA CELL GRANULOMA OF A MEDIASTINAL LYMPH NODE WITH EXTENSION TO RIGHT LUNG

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PLASMA cell neoplasms and plasma cell granulomas often cannot be separated by any satisfactory criteria. Both behave in a similar manner, showing focal and/or diffuse infiltration with complete or incomplete obliteration of the normal architecture. If the destruction is complete, a neoplastic process is often inferred, and if incomplete, it may be either process. In general, these lesions have been given neoplastic significance when encountered in the lung. Analysis of these cases shows that they may just as reasonably be granulomatous. None of the patients in the reported cases has died due to metastases.[1, 2, 3, 6, 7] Some of the extramedullary plasma cell tumors in other sites caused the death of the patient.[5] Multiple myeloma may metastasize to soft tissue.[4, 8] The following case is an example of a mediastinal lymph node infiltrated by plasma cells with extension into the adjacent pulmonary parenchyma.

CASE REPORT

Mrs. D. M. G., a 37-year-old white married woman, was admitted to the Sheltering Arms Hospital in Richmond, Va., in February, 1954. Her chief complaint concerned a density in her chest that was discovered in a routine roentgenogram, in 1942, and which was diagnosed as a tuberculous lesion. The examination had been prompted by an increasingly severe low back pain, which had been present for several years. The patient was then sent to Blue Ridge Sanitarium, from where, after six weeks of diagnostic study in which tests were negative for tuberculosis, she was discharged to her home. She had had repeated roentgen examinations at six-month intervals since her discharge in 1942, up to the present admission. She had never had symptoms referable to the lesion, other than backache. She was told in the ensuing years that the lesion as seen on the original film had not changed materially. The review of symptoms was essentially negative. A history of operations revealed that she had had a thyroidectomy in October, 1943, for thyrotoxicosis. The family and occupational history were noncontributory.

The physical examination revealed a well-developed, well-nourished woman in no apparent acute distress. She weighed 118 pounds. On admission, her temperature was 99.8° F., blood pressure 160/58, pulse 84, and respirations 24. The eye, ear, nose, and throat examinations were essentially negative. The anterior neck region contained an old, well-healed, crescent-shaped scar. The thyroid was not felt and the trachea was in the midline. The lungs expanded well and equally and were clear to percussion and auscultation. No râles or wheezes were heard. The heart sounds were of good quality, without murmurs or thrills and with a regular rate. The abdomen was flat, soft, and nontender. No masses were felt. The pelvic and rectal examinations were negative. The urine was normal except for a trace of albumin. The blood count was essentially within normal limits. One determination of plasma proteins showed albumin 4.4 Gm. and globulin 2.6 Gm. The Kline test was negative.

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Roentgenograms of the chest revealed a density in the right hilus with an increase in multiple densities of the entire right lung field. The left lung field was not involved. On comparing the 1942 films with subsequent films, no prominent change was noted from that seen on the original examination.

The bronchoscopy before surgery revealed a normal larynx, moderate blunting and widening of the carina, and no visible tumor or stenosis.

An exploratory thoracotomy was performed on the sixth hospital day. The right lung was removed along with a mediastinal tumor that involved almost all of the upper and middle lobes and a portion of the lower lobe. The postoperative course was uneventful and the patient was discharged on the twenty-third hospital day.

PATHOLOGIC FINDINGS

Gross Examination.—The specimen consisted of the entire right lung measuring 17 by 13 by 3 cm. The organ was about normal in size, shape, and weight. The pleura was generally granular and fibrous, except for the part over the lower lobe. In the upper half of the hilar region there was a crescent-shaped hollowed-out area surrounded by compressed lung tissue. This defect had been originally filled with tumor. There were many pieces of tissue received separately to make a mediastinal tumor mass measuring 4 cm. in size altogether. It was friable, white, solid tissue. There was a slightly thickened rim of fibrous tissue around the defect in the lung. The lung parenchyma showed thickened nodular areas throughout. These were fibrous and crepitation was minimal. The bronchi were patent and apparently normal except for slight thickening of the walls adjacent to the tumor. The pulmonary arteries and veins were grossly normal. The bronchial lymph nodes were enlarged, firm, and black. Several 0.5 mm. subpleural black, firm nodules were present.

Microscopic Examination.—Section of the mediastinal mass showed a lymph node largely replaced by plasma cells (Figs. 1 and 2). These cells varied slightly in size and shape. The nucleus was large and hyperchromatic in a few cells. Russell bodies were prominently seen throughout (Fig. 2). The medium-sized and small blood vessels showed a varying amount of intimal fibrosis with encroachment upon the lumen causing almost complete obliteration (Fig. 3). The pulmonary tissue was replaced by focal and diffuse plasma cell infiltration and associated with hyalinization of fibrous tissue. Sometimes eosinophilic hyaline bodies were found replacing normal pulmonary parenchyma (Figs. 4 and 5). These hyaline bodies consisted of broad eosinophilic bands. The bronchial mucosa and submucosa were infiltrated by plasma cells, but the cartilage was not invaded by the cellular infiltrate (Fig. 6).

Pathologic Diagnosis.—Plasma cell granuloma of a mediastinal lymph node with extension to right lung.

DISCUSSION

The published cases concerning these plasma cell lesions are presented in Table I. The pathology was usually found on roentgen examination of the chest. Tuberculosis was eliminated by laboratory examination of the sputum. The usual laboratory tests were used to exclude multiple myeloma, and all were negative. Kuley and Kuntman[7] found 4 per cent plasma cells in the bone marrow, but attached no significance to this finding. Russell bodies were found in slightly less than one-half of the cases. In general, the clinical course of these cases had not progressed in accordance with recurrent or metastasizing neoplasms. We feel that, due to the long duration of the illness in our case, a granulomatous process is favored over the neoplastic. It may be that, at some future date, this patient will show evidence of multiple myeloma.

Fig. 1.

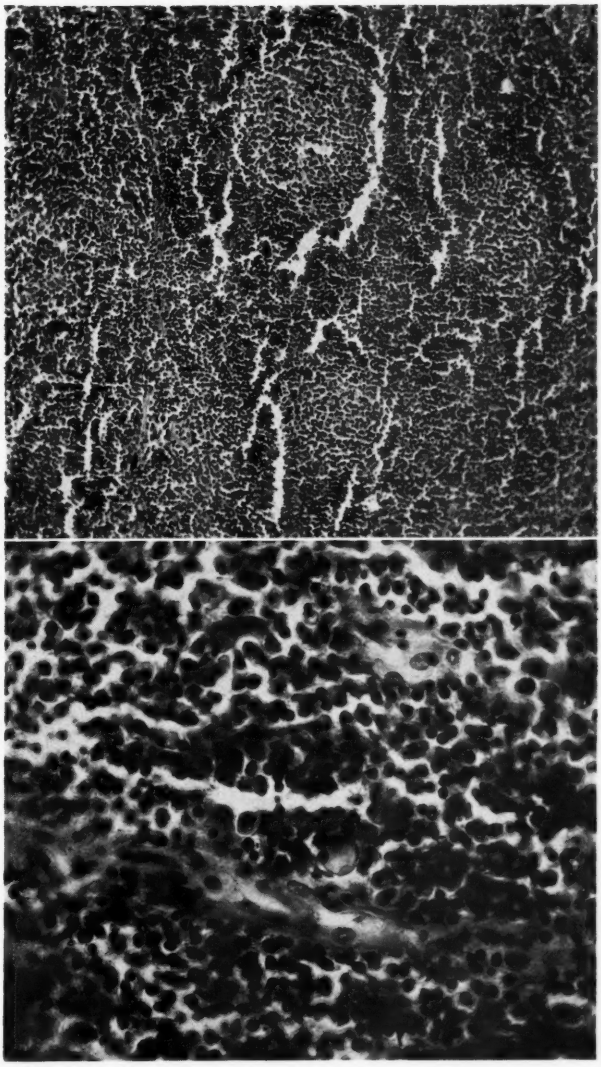

Fig. 2.

Fig. 1.—Mediastinal lymph node, low power.
Fig. 2.—Mediastinal lymph node, high power. Most cells are plasma cells, and a Russell body is in center of the field.

Fig. 3.

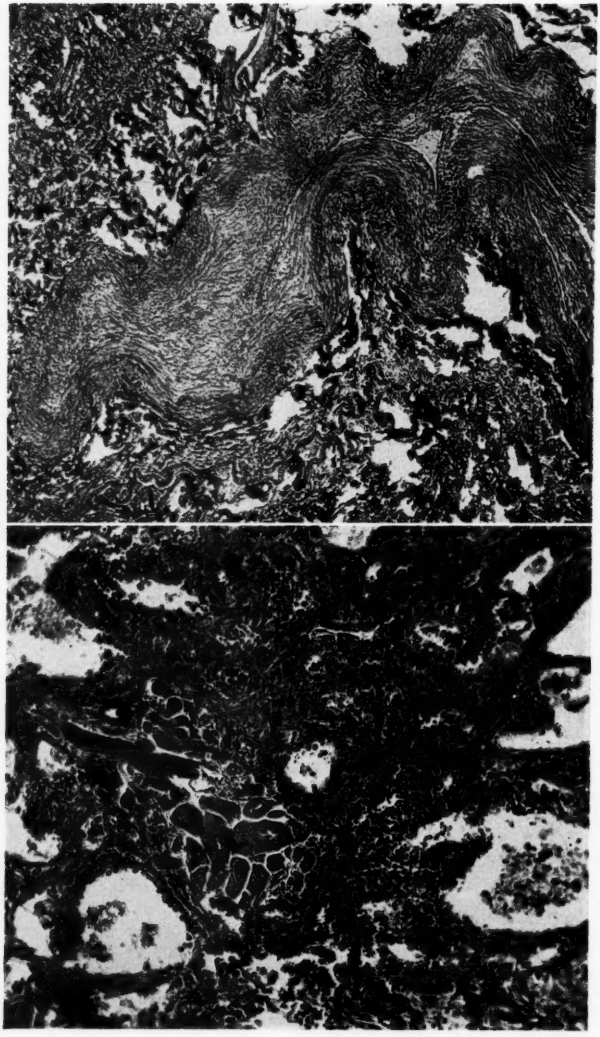

Fig. 4.

Fig. 3.—Lung, low power. Sclerosis of a large vessel due to marked intimal thickening.
Fig. 4.—Lung, low power. Granuloma associated with hyaline bodies.

Fig. 5.

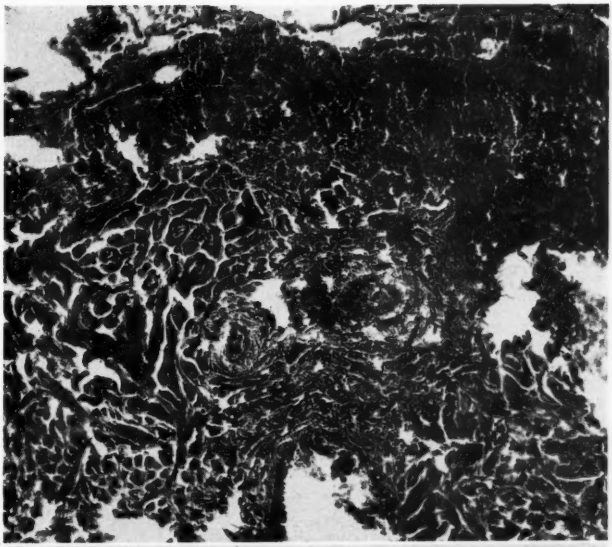

Fig. 6.

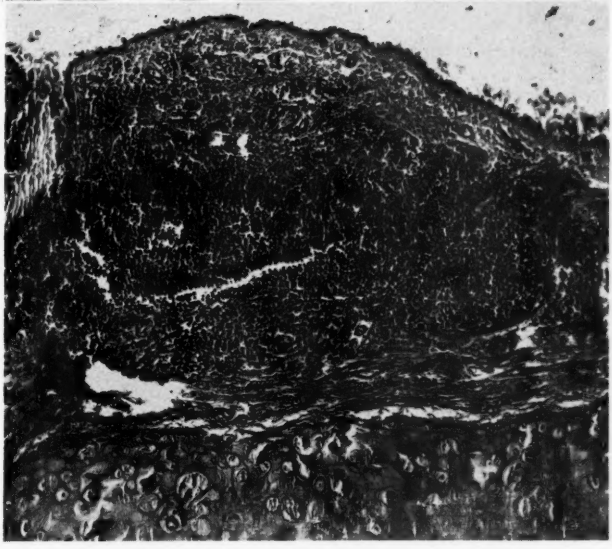

Fig. 5.—Lung, high power. Severe hyalinization of parenchyma.
Fig. 6.—Lung, high power. Diffuse sheets of plasma cells in wall of bronchus. The cartilage is not invaded.

TABLE I. REVIEW OF CASES IN THE LITERATURE

AUTHOR	AGE	SEX	ROENTGENOGRAM	PATHOLOGIC FINDINGS	AUTHOR'S DIAGNOSIS
Childress, and Addie[1]	37	M	Mass in left upper posterior mediastinum	6.5 cm. mass made up of plasma cells	Plasma cell tumor of pleura
	21	M	Mass in right middle lobe of lung	4 cm. mass containing plasma cells and Russell bodies	Plasma cell tumor of lung
Cotton, and Penido[2]	57	F	Mass in left upper lobe of lung	5 cm. mass infiltrated with plasma cells	Fibrosing plasmacytic granuloma of lung
Gordon, and Walker[3]	30	F	5 cm. mass in left upper inner lung field	5 cm. mass composed of plasma cells with Russell bodies	Plasmacytoma of lung, site of origin not determined
Hill, and White[6]	3	F	Mass filling left chest	8 cm. mass composed of plasma cells	Plasmacytoma of lung
Kuley, and Kuntman[7]	30	F	Mass in right hilus	Aspirate of mass contained 70 per cent plasma cells	Plasmacytoma of lung, site of origin not determined
Spyker, and Kay	37	F	Mass in right hilus with increased pulmonary markings	4 cm. mass containing plasma cells and Russell bodies with extension to lung	Plasma cell granuloma of mediastinum with extension to lung

There has been no roentgen or laboratory evidence of myeloma at the time of this writing. The presence of Russell bodies seems to support the contention that this is an instance of granuloma. We believe that the other six cases reported in the literature were apparently similar lesions and we agree with Dr. Fred Stewart[1-3] that most of these cases can be classified as granulomas.

SUMMARY

A case of plasma cell granuloma of the mediastinum and adjacent pulmonary tissue is reported. The lesion was present at least twelve years prior to its removal.

We desire to acknowledge Dr. W. A. Johns' permission to report his case from the Department of Surgery, Sheltering Arms Hospital, Richmond, Va.

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ARCHITECTURAL RECONSTRUCTION OF THE LUNG AFTER PARTIAL RESECTION OF PULMONARY PARENCHYMA

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COMPLETE re-expansion of the residual pulmonary parenchyma after partial resection is an essential condition for quick cicatrization, good functional recovery, and healing without the complication of empyema or bronchopleural fistula. Re-expansion depends on mechanical and anatomical factors.

An essential mechanical factor is the maintenance of patent bronchi which permits the air to reach the terminal bronchioles to ensure the ventilation of the alveoli so that maximum re-expansion of the lung may occur. To maintain re-expansion, pleural fluid must be aspirated by constant active suction.

The quality of the pulmonary parenchyma is an anatomical factor which facilitates or hinders the re-expansion. Normal pulmonary tissue is elastic and able to be distended by intra-alveolar pressure. As a result, it will usually replace the loss of substance caused by the operation. Yet, pathological types of parenchyma are frequent. The emphysematous lung, although relatively inelastic, may be distended to fill some of the remaining intrathoracic space. The fibrous lung, however, fixed by its rigid framework, has lost its elasticity, making hyperexpansion impossible. Finally the atonic lung, its texture being a mixture of fibrosis and emphysematous lesions, has no tendency to dilatation and will not occupy a space greater than it originally did. These varieties of lungs have, in other words, no tendency to play the spatial role described by Churchill, as essential in the refilling of the hemithorax after partial resection.

The analysis of the mechanism by which pulmonary tissue re-expands is based upon facts of current observation. First, the study of spontaneous healing of segmental lesions in tuberculosis shows that cicatrization is obtained by retraction. The diseased segment retracts, pulling and expanding the surrounding healthy parenchyma. The latter opens like a fan around its bronchial tree, while the diseased segment closes. This is the so-called Chamberlain's segmental clock. Furthermore, by observing the behavior of the hemithorax in children after partial resection, one is amazed at the facility with which the soft and resilient remaining parenchyma fills the thorax. Finally, the comparison between the postoperative courses of upper and lower lobectomies demonstrates the fact that the filling of the dead space poses no problem in the latter, whereas, in the former, difficulties are very often encountered.

Thus, one comes to the conclusion that three different factors play roles in the refilling of the dead space after partial resection:

1. Hyperexpansion of the residual parenchyma, possible because of the elasticity of the tissues.

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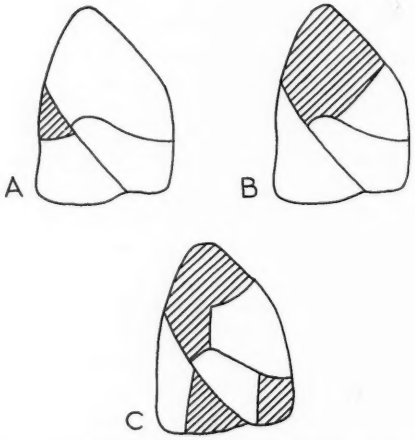


Fig. 1.—Types of resections where difficulties in refilling are encountered:
A, Resection of the superior segment of the lower lobe.
B, Resection of a large apical and posterior segment.
C, Resection of several segments.

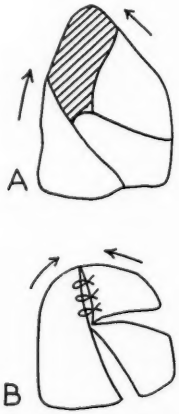


Fig. 2.—Fixation of the intersegmental resection plane of the anterior segment to the superior segment of the lower lobe (resection of the apical and posterior segments). Freeing of the fissures.

2. Elevation of the diaphragm, which, depending on its integrity, diminishes the volume of the hemithorax.

3. Displacement of the mediastinum whose mobility and whose ability to shift contribute also to the filling of the residual space.

Observation also shows that (1) it is easier for the organism to obliterate a dead space by shift of a mobile organ, diaphragm, or mediastinum, than by hyperexpansion of the parenchyma, except when the pulmonary tissue is healthy and elastic, which is rare in the adult; and, (2) when at the end of the operation, there remains a rigid parenchyma from which a pyramid-shaped portion has been removed the refilling remains a difficult problem. This is particularly true in isolated resection of the superior segment of the lower lobe and apical-posterior segment of the upper lobe. To avoid these instances, many thoracic surgeons perform thoracoplasty or plombage, either in one operative procedure with the resection or, when a residual pleural pocket is evident, as a delayed postresection thoracoplasty. Yet one must consider that this method complicates the operation, the postoperative course, and causes skeletal deformities.

These different facts led us to develop a method of architectural reconstruction of the lung which permits satisfactory re-expansion of the lung at the end of the operation and avoids the postresection thoracoplasty.

We started suturing edge to edge the raw intersegmental surfaces and then progressively elaborated a technique the basic principle of which is to bring the residual parenchyma in contact with the rigid parts of the thoracic cavity: the apex of the hemithorax and costal wall. Thus, the lung might be well separated from mediastinum and diaphragm. These mobile structures are able to shift and fill the residual space.

From this basic principle two necessary objectives have been derived:

1. The reconstruction of a pulmonary pyramid proper to be reintegrated into the bony dome of the hemithorax. We had observed that after certain partial resections of the upper lobe, after left upper lobectomy and after right upper and middle lobectomy, important pleural pockets remained in the apex. Even good parenchymal expansion could not obliterate them. Therefore, it seemed to us indispensable to reconstruct a pulmonary apex adaptable to the dome of the hemithorax.

2. The achievement of a close contact between the pulmonary parenchyma and the bony structures of the thorax, costal wall, and vertebral gutter was a logical deduction from the previously mentioned facts and to us an imperative condition for the success of the operation. It should assure complete re-expansion and a proportional recuperation.

To apply these two theoretical principles, we use certain technical procedures which will now be described.

1. The lung is completely freed from its parietal fixation (unless there remains only a small retracted lower lobe) and, if necessary, its decortication. Thus, the re-expansion will be well equilibrated, and will involve all segments which will decrease tension on the areas adjoining the operative zone.

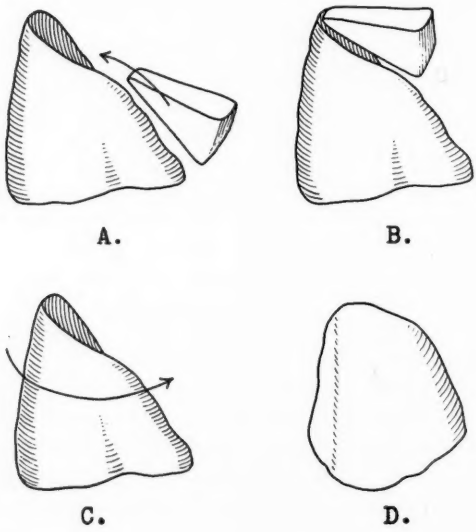


Fig. 3.—Rotation of a lobe.

A, After upper lobectomy the fissure between the middle and lower lobes is opened.

B, The posterior rim of the middle lobe is brought in contact with the apex of the superior segment of the lower lobe.

C and *D*, By rotation around its hilar axis the lower lobe is placed so that the posterior surface becomes lateral.

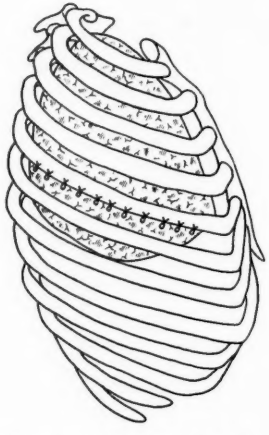


Fig. 4.—Once turned around its axis the lower lobe is pushed upward so that it will fill the apex of the hemithorax. It is maintained in this new position by a few fixation stitches to the chest wall.

2. The opening or the completion of the interlobar fissures has the same objective as the freeing of the lung, an equal distribution of the tension each lobe has to support. It will allow the bronchial tree to open and to distribute to each of its elements the corrective role of refilling the dead space.

3. The rotation of a segment or a lobe around its bronchial axis brings it in the required new position. This rotation must be done smoothly, avoiding, naturally, any kinking of blood vessels, allowing the vascular system to preserve its functional integrity. Surprising as it may seem, this rotation is in reality only a slight exaggeration of what nature does in its slow and spontaneous process of retraction when a lobe becomes atelectatic or carnified, the adjoining parenchyma replacing the loss of substance. It is also the process which occurs spontaneously to compensate for loss of pulmonary tissue after partial resection. We have verified this by bronchography in two collateral series of cases.

Fig. 5.

Fig. 6.

Fig. 5.—Bronchogram after right upper lobectomy.
Fig. 6.—After rotation and upward displacement, the middle lobe, hence, constitutes the apex of the lung. The bronchial tree has unfolded.

4. The fixation of the rotated lobe or segment in this new position is a complementary procedure to maintain the acquired position. This is done by a series of stitches fixing the raw intersegmental or interlobar surfaces together. The stability obtained by this architectural reconstruction shifts the hyperexpansion away from the operative area.

If necessary, we conclude the endothoracic procedure by securing the lung to the chest wall with a few stitches. A close contact will be assured between lung and chest wall even if a dead space has to be left near the mediastinum or diaphragm. We mentioned before that it seemed very important to us to fill the apex of the thoracic cavity with parenchyma and this is easily possible if the lung, remodeled in the form of a cone, is pulled upward. This procedure is indispensable in the resection of part of or the whole upper lobe and a suspension by suturing is always necessary here.

5. All of these manipulations must be done with the lung well inflated. Only the pressure given by the anesthetist's balloon, transmitted to the alveoli, allows one to judge how to place lobes and segments and assign them the optimum definitive place.

This theoretical discussion, abstracting the different technical points, can be applied to almost all cases. Yet it seems useful to develop with more detail certain particular instances.

There follow three examples:

1. After right upper lobectomy or resection of the apical-posterior and anterior segments in the left, the lower, and middle lobes or the lingula, there is difficulty with expansion to fill the dead space in the adult. To re-create an apex, we open completely the fissure between the lower and middle lobes. The middle lobe or lingula is then drawn backward and upward until its posterior angle reaches the top of the superior segment of the lower lobe. This requires rotation around its hilar axis. The middle lobe is fixed with a few stitches to the lower lobe in this new position and will henceforth constitute the pulmonary apex.

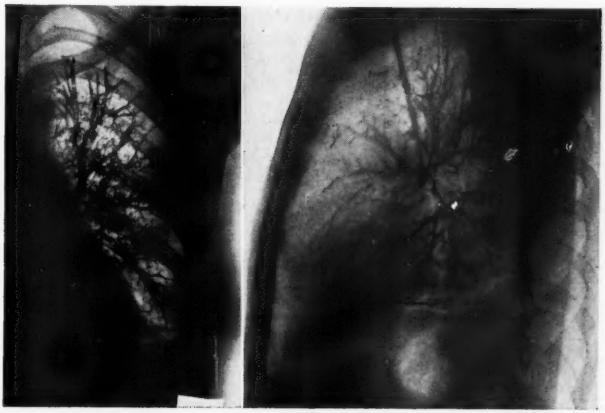
2. After resection of the apical and posterior segments, or the apical-posterior segment, we often free the great fissure between the right lower and middle lobes or left lower and upper lobes. We then slide the remaining parenchyma of the upper lobe backward until the raw resection plane comes in contact with the posterior edge of the lower lobe. As after upper lobectomy, a few stitches secure the lobes in their new position.

3. After right upper and middle lobectomy, or total left upper lobectomy, we section the triangular ligament which fixes the lower lobe and turn the latter around its hilar axis so that its posterior surface becomes lateral. The lobe is then pushed upward and is fixed to the thoracic wall. It fills the dome of the hemithorax. This suspension leaves the lower lobe distant from the diaphragm and mediastinum especially when it is a small-sized lobe.

The results we have obtained with this method have always been good even in cases of fibrotic lungs. It is evident that this technique does not change the usual postoperative care that is required. An atelectasis might well tear the lung loose from its fixations. The postoperative surveillance must be as constant as in routine procedures and any bronchial obstruction or air accumulation in the hemithorax avoided or corrected immediately. We have operated thus on 136 patients during the last twenty months; 14 resections of a single segment, 58 resections of two or more segments, and 64 lobectomies for tuberculosis, bronchiectasis, residual abscesses, cysts, etc.

We have observed residual pockets following atelectasis in seven instances. Among these we noted four cases of localized empyema, three of which were easily cured, the fourth required further surgery. The three remaining cases, complicated with atelectasis, produced only simple air pockets. If it is difficult to hold our method responsible for these complications, one can nevertheless argue that it did not prevent them.

Bronchograms with Lipiodol were made in 30 of our patients between the twelfth and twenty-first postoperative days to visualize the changes of the bronchial system after the structural modifications to which it had been subjected. These radiologic checkups never revealed any bronchial kinking. Some showed incurvations similar to those observed after spontaneous retraction



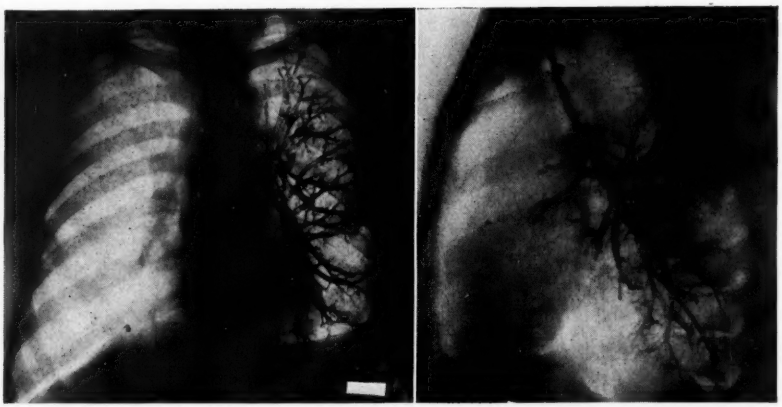
Figs. 7. and 8.—After left lower lobectomy, the upper lobe has rotated slightly. The lingula occupies now the lateral part of the hemithorax. Note the incurvation of several small bronchi.

Figs. 9. and 10.—After resection of the anterior segment the apical segment has been fixed to the middle lobe by a few stitches. The middle lobe bronchus is slightly curved.

in tuberculosis; others were in all points comparable to the bronchograms studied by J. Antrim Crellin, J. Stauffer Lehman, Daniel Mason, and J. L. Curry after partial lung resection. We observed mostly, on bronchograms made after lobectomy, a harmonious fanning out of the bronchial tree into its new area.

One might question theoretically, whether the artificial reconstruction of the parenchyma is justified and whether one is justified in modifying a

natural architecture, to impose new forms and positions to segments or lobes without risk of functional incapacitation. One can object that the fixation of the segments to one another, the fixation of the lung to the skeleton, in order to provide enlargement might interfere with the physiologic role of the lung and disturb the respiratory function. Up to the present, we have not made any detailed functional evaluations which might justify our technique, but



Figs. 11. and 12.—Resection of the apico-posterior and anterior segments. The lingula is now in the apex.

Fig. 13.—Resection of the apical and posterior segments of the right upper lobe. The fissure between upper middle and inferior lobe has been opened.

the excellent clinical results obtained, the normal postoperative films, and the radioscopic study which reveals normal aeration, have encouraged us to continue with our method. The fixation of the lung to the thoracic wall seems therefore not to be a serious handicap. The parietal adhesion of the lung is an inevitable consequence of every thoracotomy. The free sliding motion of the lung within the thorax, normal movement of any free parenchyma, disappears

after all endothoracic operations and we do not think that the fixation to the chest wall with a few stitches changes anything. As to the change in the positions of segments or lobes, the slight incurvations of bronchi still allow perfect air circulation and the fact that they exist cannot be considered the consequence of the method alone.

The air leaks which one might expect to increase, because of the fixation stitches which damage the lung, have never been more significant than after routine procedures. They always stay within normal limits. The pleural pockets left near the diaphragm or mediastinum have always been obliterated in forty-eight hours by the molding of these mobile organs to the re-expanded residual parenchyma.

It is evident that this technique can be applied only when the remaining parenchyma is sufficient to refill the hemithorax. It is of no help if the residual lung is too small or insufficient. Two residual segments cannot refill a hemithorax in an adult.

Nevertheless, in many cases, the method has allowed us to refill a thoracic cavity perfectly; this could otherwise not have been achieved. We think that the architectural reconstruction of the lung is of great practical help and is theoretically justified.

SUMMARY

1. The re-expansion of the lung after partial resection is essential for the success of the operation.

2. To avoid postoperative complications and assure functional recuperation, this re-expansion must be complete. This depends on mechanical and anatomical factors.

Three mechanisms play roles in the refilling of the hemithorax: hyperexpansion of the remaining parenchyma, elevation of the diaphragm, and shift of the mediastinum.

4. Observation shows that there is no difficulty if after the operation the remaining lung is in contact with the rigid elements of the thoracic cavity (ribs and vertebral gutter) and distant from the mobile structures (diaphragm and mediastinum).

5. To ensure the refilling of the hemithorax, the basic principle of our technique is to bring the lung in close contact with these bony structures, leaving it distant from the mediastinum and diaphragm.

6. This technique requires a few procedures which allow an architectural reconstruction of the pulmonary parenchyma to a cone-shaped entity: complete freeing of the lung, freeing of the fissures, rotation of a segment or a lobe, fixation by stitches of segments and lobes one to another and, if necessary, fixation of the lung to the chest wall.

7. This method was used in 136 patients in lobectomies and segmental resections for various indications.

8. Postoperative bronchograms never showed bronchial kinking but only wide incurvations.

9. There seem to be no theoretical objections to this method.

EOSINOPHILIC GRANULOMA OF THE LUNG

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INTRODUCTION

EOSINOPHILIC granuloma is a rare disease of unknown etiology which affects a multiplicity of tissues. While usually generalized, solitary involvement of bone,[52, 64, 76] of skin,[27] of the gastrointestinal tract,[12, 89, 100] and occasionally of other tissues[68] has been recognized. It has only recently been appreciated, however, that solitary involvement of the lung may also occur, and only two such reports can be found in the literature.[30, 67] It seems, therefore, appropriate to report a case recently encountered by us of eosinophilic granuloma of the lung without other demonstrable systemic disease.

CASE REPORT

D. B. W. (X12011), a 15-year-old white boy, was admitted to the Diseases of the Chest Hospital of the City of Hope Medical Center on May 12, 1953, because of the findings by a Mobile Unit chest x-ray survey in December, 1952, of extensive infiltration throughout both lung fields (Fig. 1). He was completely asymptomatic, without cough, expectoration, or hemoptysis. There was no fever, night sweats, loss of weight, weakness, fatigue, or dyspnea, and no frequency of urination, bone or joint pains, or skin lesions. He was admitted with a presumptive diagnosis of bilateral advanced pulmonary tuberculosis.

Past history included measles, and an unexplained episode of fever associated with left hip pain at the age of five, which lasted intermittently for one year.

Physical examination revealed a well-nourished, well-developed white boy, 15 years of age who appeared to be in excellent health. The temperature was 98.6°; pulse, 84; respiration, 22; blood pressure 120/76; height, 5 feet 9½ inches; the weight was 156 pounds. The skin was clear and there was no cyanosis. The eyes showed no exophthalmos. The oral mucosa, tonsils, and pharynx were clear. There was no cervical, axillary, or inguinal lymphadenopathy. The chest was symmetrical and expansile. The lung fields were resonant. Slight generalized accentuation of breath sounds was noted. No râles were present. The heart was normal. The liver and spleen were not enlarged. Rectal examination revealed no abnormalities. No skeletal tenderness or deformity was observed, and neurological examination was normal.

Laboratory Findings.—Blood count: The red blood count was 4,600,000; hemoglobin, 14 Gm.; white blood count was 9,800; segmented polymorphonuclear leukocytes 69, lymphocytes 21, monocytes 4, eosinophils 6. *Urinalysis:* specific gravity 1.026; albumin negative; glucose negative; acetone negative; microscopic examination revealed a few hyaline casts. *Bone marrow examination:* No abnormalities. *Sedimentation rate:* 19 mm. per hour. *Blood chemistries:* Fasting blood sugar 90 mg. per cent; nonprotein nitrogen 30 mg. per cent;

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total protein 7.4 Gm.; albumin 4.8 Gm.; globulin 2.6 Gm.; calcium 11 mg. per cent; phosphorus 3.7 mg. per cent; cholesterol 140 mg. per cent; cholesterol esters 70 per cent; amylase 32 units; bromsulfonphthalein (5 mg./kg.) 8 per cent dye retention after 45 min.; thymol turbidity 3.5 units; alkaline phosphatase 5.9 units (Bodansky); icteric index 6 units; quantitative van den Bergh test less than 0.25 mg. *Thorn test:* 75 per cent drop in circulating eosinophils. *Bacteriology:* there was no sputum raised; nine gastric examinations were negative on culture for acid-fast bacilli. Culture and smear of pulmonary biopsy specimen (including special procedures for fungi) revealed no organisms. A Mazzini test was negative. *Coccidioides serology:* complement fixation 2 plus in 1:2 dilution, precipitin test was negative, findings were considered equivocal. *Skin tests:* the Mantoux test was 4 plus in 1:10,000 dilution; coccidioidin test was negative in 1:1,000 dilution; histoplasmin was negative. *Stool examination:* negative for fat, undigested muscle fiber, and starch granules. *Electrocardiogram:* normal. *Vital capacity:* 3,700 c.c.; 72 per cent of normal. *Breath holding time:* 72 seconds.

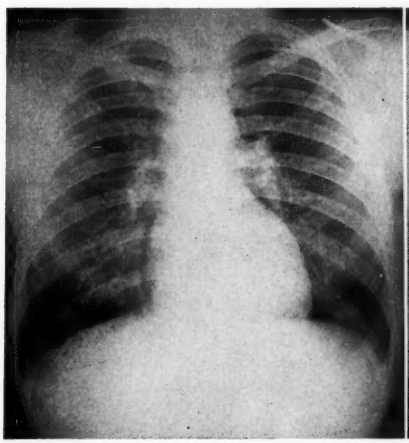

Fig. 1.

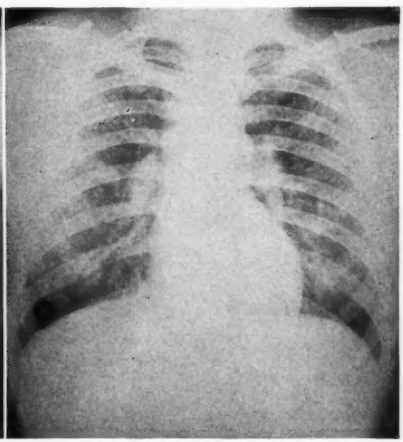

Fig. 2.

Fig. 1.—X-ray of chest shortly after discovery of the disease. Note diffuse soft nodular infiltration and suggestion of fibrocystic changes.

Fig. 2.—X-ray of chest prior to operation, showing some progression of the infiltrative process.

Clinical Course.—Despite modified bed rest at home for two months, the admission film showed an apparent progression of the pathology throughout both lung fields (Fig. 2). There were heavy root shadows and scattered mottling by soft nodular densities and areas suggestive of multiple small cystic areas or cavities from the apex to the base bilaterally. The patient was placed on strict bed rest and an antibiotic regimen consisting of streptomycin 1 Gm. twice weekly and para-aminosalicylic acid (PAS), 12 Gm., and isonicotinic acid hydrazide (INH), 150 mg., daily. Repeated examinations of gastric contents were negative for acid-fast bacilli, and the patient remained completely afebrile and asymptomatic. Bronchoscopy was performed and revealed diffuse erythema of the mucosa, but was otherwise normal. Scalene fat pad and lymph node biopsies were performed and showed no evidence of nodular or granulomatous lesions.

In view of the failure to recover the tubercle organism, it was felt that exploratory thoracotomy and lung biopsy were indicated to establish a definite histologic diagnosis, and this was performed on Oct. 2, 1953. At operation through a right anterolateral approach

through the fourth interspace, the pleural cavity was found to be free of adhesions or fluid. Small cystic areas containing air, the largest measuring approximately 1 cm. in diameter, were scattered over the surface of the lung; and on palpation, shottylike nodules from 0.3 to 0.7 cm. in diameter were felt scattered diffusely throughout the parenchyma. There was no hilar adenopathy. A biopsy specimen 3 cm. in width was taken in wedge fashion from the upper lobe, and a second similar specimen was removed from the middle lobe. Postoperative convalescence was completely uneventful.

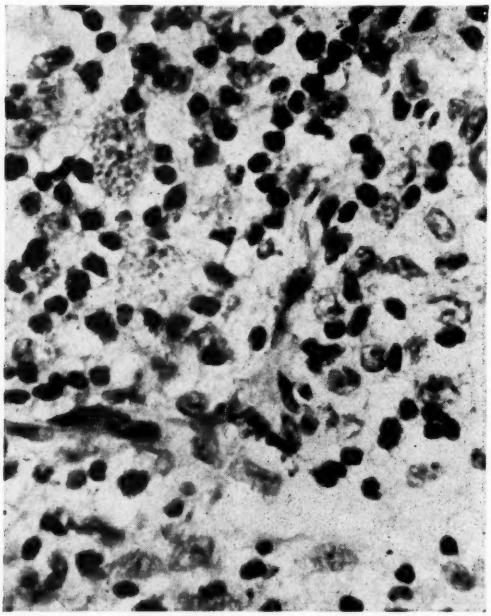

Fig. 3.—Photomicrograph of biopsy specimen, high power, showing histiocytic infiltration, profusion of eosinophiles, xanthomatous degeneration of histiocytes, phagocytosis of pigment granules by histiocytes, and fibroblastic proliferation.

Pathology Report.—Gross: The first biopsy specimen was a small wedge of peripheral lung parenchyma which included a dilated bronchial branch which led into an empty thin-walled multicystic area, and was lined by a glistening grayish-white surface a little thicker than the normal visceral pleura, with loculations up to 0.6 cm. in diameter. The second biopsy specimen was a small wedge of crepitant pink peripheral lung parenchyma containing several thin-walled empty glistening cystic areas, up to 0.4 cm. in diameter, without obvious bronchial connection. The walls of the cysts offered increased resistance to cutting despite their thinness. *Microscopic:* The histologic appearance of both specimens was similar (Figs. 3 and 4). The pleura was slightly thickened. Throughout the lung parenchyma there were aggregates of large fusiform or stellate-shaped histiocytes with vesicular nuclei, intermixed with abundant eosinophils. Occasional giant cells were noted. Small collections of brownish granular pigment were noted within some histiocytes. While in some places the aggregates of histiocytes, eosinophils, and giant cells were within the alveoli, for the most part they replaced normal lung parenchyma. Several of these nodular areas showed varying amounts of fibrosis, and in several places there was extensive fibrous replacement of the lung

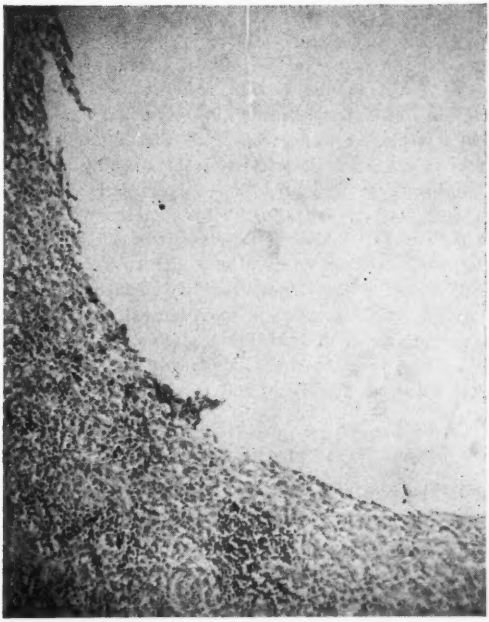

Fig. 4.—Photomicrograph of biopsy specimen, lower power, showing cyst wall.

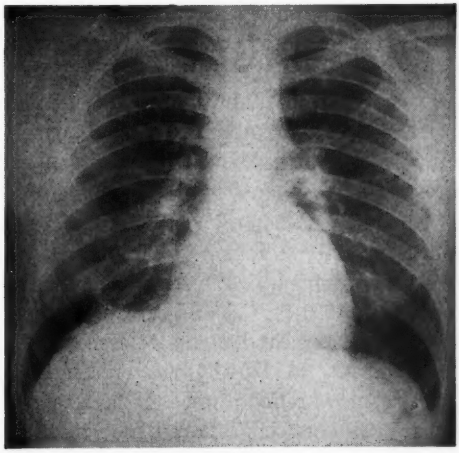

Fig. 5.—X-ray of chest nine months postoperatively and nineteen months after discovery of disease. There is slight clearing of the infiltrative process. Postoperative tenting of the right diaphragm has occurred.

parenchyma, with only a few histiocytes or eosinophils recognizable. In places, the lung parenchyma showed emphysema or cystlike spaces lined by fibrous or granulomatous tissue. Occasional bronchiolar branches led into these cysts. Diagnosis: Eosinophilic granuloma, lung.

Subsequent course: Following establishment of the diagnosis, a complete bone survey was performed, but failed to disclose any abnormalities. Because of reports[5, 7] in which it was felt that cases of Letterer-Siwe's disease had been ameliorated by antibiotics, it was decided to treat this patient with a course of combined antibiotic therapy. He had already received streptomycin 1 Gm. twice weekly for three months, as well as PAS and INH. He was now given repository-type penicillin 600,000 units daily, streptomycin 1 Gm. daily, and Aureomycin 250 mg. 4 times daily for the next three months, following which he received erythromycin 250 mg. 4 times daily for the next two months. The last x-ray examination made of his chest, nine months postoperatively and nineteen months after the disease was first noted, revealed some slight decrease in the extent of the bilateral infiltration. Postoperative tenting of the right diaphragm from pleural adhesions was present. There was no evidence of a new process or of recent spread (Fig. 5). The patient was discharged to his home and was leading a normally active life twenty months after the disease was first noted. He was asymptomatic at that time, and continued to show no evidence of extrapulmonary involvement.

DISCUSSION

It is now convincingly established that the pathological basis of eosinophilic granuloma,[23, 33, 36, 64, 76] Hand-Schüller-Christian syndrome (lipogranulomatosis or normocholesteremic xanthomatosis),[13, 14, 17, 46, 54, 81, 82, 85, 86] and Letterer-Siwe's disease (reticuloendotheliosis or histiocytosis),[1, 61, 90] is fundamentally the same.[28, 29, 42, 44, 47, 49, 52, 53, 63, 64, 66, 94, 95, 96] Lichtenstein's paper[63] is particularly definitive on the subject. Pulmonary manifestations in these conditions have usually been recorded as incidental findings in a generalized disease process in which the diagnosis of the pulmonary lesion was either inferred from positive extrapulmonary tissue biopsy, or proved at autopsy.[1-4, 6, 8, 10, 11, 13-15, 18-23, 25, 26, 29, 31, 34, 35, 37-39, 41, 43-46, 48-52, 56-60, 62, 65, 68, 69, 71-75, 77-81, 83, 84, 87, 88, 90-93, 96-99, 102-104] In only a few cases have the pulmonary manifestations themselves been the focus of interest. Actual confirmation of the pulmonary pathology in the living subject by lung biopsy, in cases where extrapulmonary manifestations existed, has been reported only 6 times.[8, 35, 63, 66a]

Clinical recognition and pathological confirmation by lung biopsy of the existence of eosinophilic granuloma as an *isolated* disease entity of the lung, without other demonstrable systemic involvement, was first reported by Farinacci, Jeffrey, and Lackey, in 1951.[30] (Their 2 cases were re-reported by Lackey, Leaver, and Farinacci, in 1952,[58] and again referred to by Lichtenstein, in 1953,[63] and Forsee and Blake, in 1954.[35]) Mazzitello, in 1954,[67] reported 2 new cases. The present report is believed to be the fifth reported case of isolated pulmonary involvement. It must be assumed, not that the disease did not exist in primary pulmonic form in the past, but that in the absence of characteristic systemic lesions by which the pulmonary lesions could be recognized, the disease process in the lungs was incorrectly interpreted. As yet, to the best of our knowledge, there has been no report of a case starting out exclusively

with pulmonary involvement and subsequently developing generalized disease. Eventual recognition of this missing link is to be anticipated.

CLINICAL FEATURES

Eosinophilic granuloma involves tissue either in the form of discrete nodular masses of granulomatous tissue of varying dimensions, or in the form of diffusely disseminated granulomatous tissue. In the larynx, fibrotic strieturing may occur following cicatrization of the granulomatous lesion therein. In the tracheobronchial tree, polypoid and papillary protrusions of granulomatous tissue have been described,[35, 81, 82] which may produce gross bronchial obstruction. Diffuse plaquelike involvement of the respiratory mucosa of the tracheobronchial tree has also been noted, and strieturing may occur at any point. Mediastinal and hilar lymphadenopathy may be extensive. The pleura is often found studded with granulomatous nodules, but may be involved in a diffuse plaquelike manner. The pulmonary parenchyma proper may be involved by a few large single or multiple nodules, but more often there is a profusion of nodules of smaller size, commonly ranging from miliary proportions to 2 cm. in diameter, giving the tissue a characteristic "shotty" feel. Diffuse granulomatous infiltration of the interstitial parenchyma is also usually present, and in later stages parenchymal fibrosis becomes advanced. Going hand in hand with these changes are the cystic changes which result from bronchiolar obstruction, produced by actual granulomatous obturation of bronchiolar lumina and by cicatricial constriction and stenosis of the lumina following interstitial fibrosis. Granulomatous degeneration of the alveolar wall may be an accessory factor in cyst formation. These cystic changes may range from a few small surface blebs, through increasing emphysematous degeneration, to complete cystic degeneration with giant bullae or honeycombed lungs in the end stages.

Microscopically, the pathologic features of the disease are classically subdivided into four phases on the basis of progressive age:[49]

1. In the hyperplastic-proliferative phase, there is accumulation of histiocytes, which appear in strands and sheetlike collections. Some are actively phagocytic and some are multinucleated. There is an associated inflammatory cell infiltration consisting primarily of eosinophilic polymorphonuclear leukocytes, but including plasma cells and round cells in lesser numbers.

2. In the granulomatous phase, there is increased growth of blood vessels and stroma in the area of histiocytic proliferation. Fibroblastic activity is noted, and reticular fibrils are laid down. The previously noted inflammatory cell infiltration composed primarily of eosinophils is conspicuous, and giant cells may be noted. Areas of hemorrhage and necrosis may be found.

3. In the xanthomatous phase, isolated histiocytes or nests of histiocytes undergo transformation into foam cells.

4. The fibrotic phase is the end phase, or that of healing. Cellularity of the pathologic picture diminishes as fibrosis increases. Fibrosis is noted to some extent in all stages, but eventually becomes quite pronounced.

There is no strict demarcation between the different stages and much overlapping occurs. The same pathological specimen may show different pictures in different areas, and elements of all may be found in any one field.

The disease may be present at any age, and in both sexes. The patient with pulmonary involvement may be completely asymptomatic, as was the patient reported in this paper. On the other hand, he may complain of chronic productive cough, bloody streaking of the sputum, or at times frank hemoptysis. Low-grade fever may be present, more marked in the afternoon and asssociated with night sweats. Weakness, fatigability, and weight loss are constitutional concomitants. Chest pain may be present. Pleural effusion may occur. Spontaneous pneumothorax, frequently bilateral, may occur following the rupture of emphysematous blebs. Dyspnea of increasing severity may be present, and as the disease progresses respiratory decompensation may become extreme. In addition, progressive right heart failure may eventually result from the extensive pulmonary fibrosis.

In early stages, chest x-ray films may show a generalized reticulation associated with miliary mottling, and later there may be diffuse soft nodular infiltrations of varying dimensions. Large irregular densities may be seen. Fibrotic changes are a constant feature, and, in the end stages, fibrosis may become extreme. Perhaps the most interesting changes are the cystic ones, which may vary from a few fine scattered cystic reticulations through generalized emphysema to bullous degeneration or advanced honeycombing. Cysts containing fluid which alternately fill and empty, thus presenting a striking picture on serial x-rays, have been reported.[35] The effects of gross bronchial obstruction, with localized emphysema followed by atelectasis and pneumonitis, may be noted. There may be extensive mediastinal and hilar lymphadenopathy.[25]

No characteristic laboratory findings have been noted. Blood counts occasionally reveal a transient eosinophilia. Bronchoscopy in our case and in one of Mazziotti's revealed diffuse mucosal erythema.

Eosinophilic granuloma of the lung must be differentiated from tuberculosis; sarcoidosis; silicosis, asbestosis, and other pneumoconioses; coccidioidomycosis, histoplasmosis, and blastomycosis; Hodgkin's disease and other lymphomas; and the various types of fibrocystic disease of the lung including congenital fibrocystic disease associated with pancreatic fibrosis, and idiopathic pulmonary fibrosis with emphysema. When history, sputum studies, skin tests, serologic tests, roentgenograms, bronchoscopy, and node or fat pad biopsies have failed to yield a definitive answer, then lung biopsy, a relatively innocuous procedure, should be performed in order to make a conclusive histologic diagnosis. We have preferred a small formal anterolateral thoracotomy under intravenous Pentothal anesthesia with endotracheal intubation and oxygen administration, for more adequate examination of the lung and more accurate selection of tissue to be biopsied. However, the simplicity of Klassen's[55] method of lung biopsy has much to recommend it.

There is no established effective therapy for eosinophilic granuloma of the lung. The classical modality is x-ray therapy, and although good results have been reported with its use,[4, 51, 103] the effect has usually not been striking.[16, 23, 58] ACTH and cortisone should theoretically reduce the extent of the interstitial fibrosis,[6, 70] but little actual improvement has been noted following their use.[8, 11, 48, 58, 68] Chemotherapy with nitrogen mustards has been advocated.[9] Perhaps the most recent approach to this problem is that of antibiotic therapy. Aronson[5] reports remarkable clearing of the process of Letterer-Siwe's disease with streptomycin therapy, and Bierman and associates[7] report amelioration in the same disease using combined antibiotics. In the case reported herein, slight clearing followed antibiotic administration. It must of course be recognized that natural remissions have been reported without therapy.[58, 79, 104] Since the disease is generalized, there can never be any indication for primary pulmonary resection. However, palliative surgery may occasionally be considered in selected cases of bronchial stenosis or obturation of the bronchus with granulomatous tissue, in cases of giant bullous degeneration of the lungs, and in cases of repeated spontaneous pneumothorax with incomplete re-expansion of the lung.[8, 66a]

The prognosis must be guarded in all cases. In general, the older the patient at the time of onset, the more benign is the course. While the prognosis is apparently better when only one tissue is involved, observation over a prolonged period of time is necessary to rule out the onset of foci elsewhere. A progressively severe course may usually be anticipated, with increasing pulmonary fibrosis and cystic transformation of the lung, and terminal cor pulmonale. Nevertheless, the disease may remain stationary for long periods of time, and spontaneous remission may occur. Cases of generalized systemic involvement with pulmonary lesions remaining asymptomatic for as long as ten years after onset have been reported.[98] The prognosis for primary pulmonary lesions cannot be stated.

CONCLUSIONS

1. A case of primary eosinophilic granuloma of the lung without other demonstrable systemic involvement is presented, representing, we believe, the fifth reported case.

2. The disease is characterized by striking fibrotic and cystic pulmonary degeneration.

3. Eosinophilic granuloma should be considered in the differential diagnosis of nodular, infiltrative, and fibrocystic disease of the lung.

4. Lung biopsy is an essential diagnostic procedure in such cases.

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INDUCTION OF BRONCHIAL CANCER BY LOCAL MASSING OF CARCINOGEN CONCENTRATE IN OUTDRIFTING MUCUS

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INHALED CARCINOGENS

THE danger in inhaling cigarette smoke lies in the smallness of the particles, for this ensures that many if not most of them are carried to the rich capillary net of the delicate alveolar walls where the diffusible product is immediately absorbed to give the smoker his "kick." It is to get this effect that he inhales. If the smoke is held in the lungs long enough there is little or none of it visible in the exhalation. But not all of the elements of the smoke are thus promptly absorbed, and tarry ultramicroscopic materials remain on the alveolar walls, doubtless temporarily entrapped in the alveolar mucoid fluid (Macklin[8, 9]), and are speedily accumulated in the segregation apparatus of the phagocytic pneumonocytes (alveolar phagocytes). These "dust cells" make their way to the glottis to be swallowed or spat out. They are of the same category as heart failure cells. In smoker's sputum their segregation granules appear brownish in color. The dust cells probably never burrow out of the alveoli to enter the lung interstices and lymphatic vessels as some writers used to suppose (Macklin[10]). But only a fraction of the dust cells reach the glottis intact; most of them disintegrate and their contents are borne along in the magic carpet or raft of mucus that constantly moves from the alveolar region along the bronchial system to the trachea and glottis. This carpet is motivated by millions of underlying ciliary fingers waving sedulously outward. It is a vital escalator for without it the lungs would soon fill with inspired dust.

Now the smoke derivatives, thus infesting the surface of the lung interior, both outside and inside the dust cells, are carcinogenic. Wynder, Graham, and Croninger[4] have told us how cigarette smoke residue, painted on live mouse skin, induces cancer there. The mucus carpet is charged with this carcinogen. Part of it doubtless never enters the dust cells at all but is picked out of the smoke by the sticky bronchial walls before it enters the alveoli. Graham[4a] has pointed out that 90 per cent of all bronchial cancers are of the epidermoid (squamous-cell) type and that it is very rare in nonsmokers.

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THE TRIANGULAR ESCALATOR

To visualize the diagrammatically deltoid form of this gliding mucus raft which may be so dangerously infiltrated with cancer-producing eliminates, we must imagine the bronchial tree as split open, its walls flattened out, and sections of equivalent caliber laid side by side (Macklin and Macklin[12]). This feat would be impossible practically, but in imagination it may be accomplished. It is dramatically clear that the peripheral alveolar part of this field is immensely greater than the hilar part, being one hundred square meters or one million square centimeters in area (von Hayek[14]) as compared with but a few square centimeters. With such a discrepancy, we would be unable to represent the two in a realistic drawing, but by imaginatively shrinking the peripheral part we may construct a practical diagram, as has been done in Fig. 1, which epitomizes the main point of this discussion, namely, that as the carpet moves from base to apex of the triangle its streams converge and its contents become concentrated. By using ellipsoidal contours, an attempt has been made in Fig. 1 to suggest the enormously greater area of the peripheral region as contrasted with the stem, so that instead of a triangle one has something more like the transection of a renal pyramid.

CONVERGING CURRENTS

The peripheral alveolar zone is, in inhalers, the main "catchment basin" of smoke-carried carcinogens. It is composed of all the alveolar air surfaces put together. In cigarette smoke inhalation, a heavy shower of tarry particles falls upon it. These are really smog particles for, from the warm humid air of the respiratory tract, each grain gathers up an investment of water molecules. These grains, after impingement on the alveolar wall, are moved centrally, and it would seem mainly within dust cells and probably by amoeboid movement, first to the stems of the lung lobules constituted of the transitional (respiratory) bronchioles (Macklin[9]). This first lap of the journey has entailed the most spectacular narrowing of the carpet which, up to this point, has been aqueous-mucoid (Macklin[9]) rather than mucous in type. There is no apparent ciliary motivation here.,

THE VULNERABLE HILAR EPITHELIUM

We may, then, imagine this gradually narrowing raft, in which lurk carcinogens, as drifting from the periphery of the lung toward and into the hilus. Each part of it must pass consecutively along the alveolar bronchioles (ducts, Macklin[9]), transitional (respiratory) bronchioles, various orders of smooth-walled bronchioles, and then the small, medium, and large bronchi. The reason the raft is continuously narrowing is because it has to adapt itself to the extent of the wall space of each class of air tube and this collective wall area is reduced rapidly. The collective cross section and hence width of the spread-out wall mucosa of all the small bronchi, for instance, is greater than that of all the medium bronchi and, in like mode, there is surface diminution on down to the trunk of the bronchial tree. We may ask why the raft does not

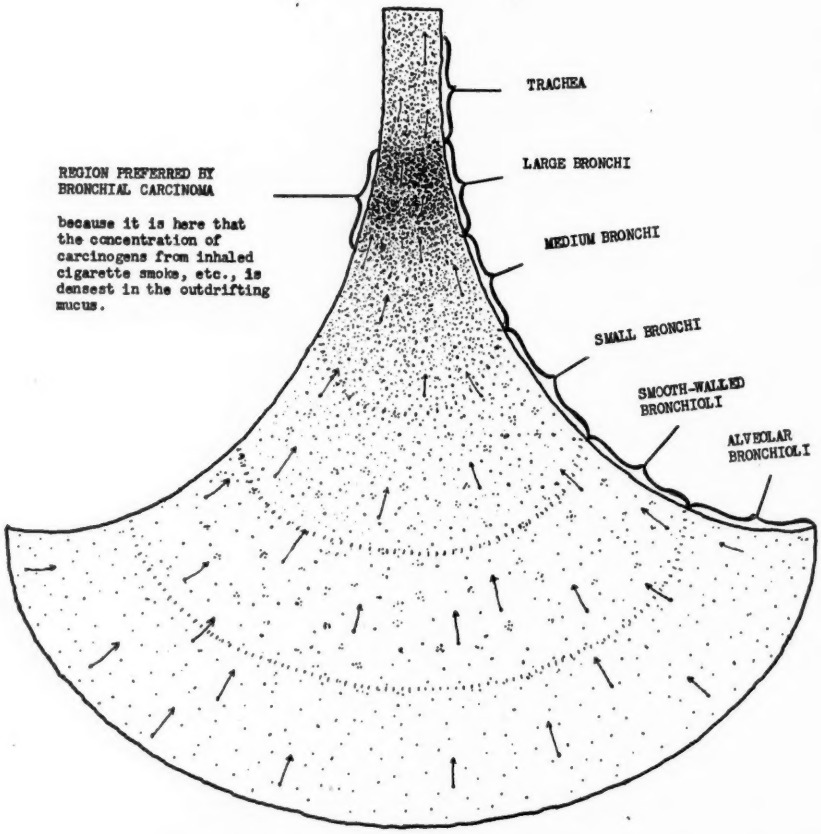
TRACHEA
LARGE BRONCHI
REGION PREFERRED BY BRONCHIAL CARCINOMA
because it is here that the concentration of carcinogens from inhaled cigarette smoke, etc., is densest in the outdrifting mucus.
MEDIUM BRONCHI
SMALL BRONCHI
SMOOTH-WALLED BRONCHIOLI
ALVEOLAR BRONCHIOLI

Fig. 1.—The "Carcinogenshed." An idealized conception of the surface drainage field of the interior of the lungs to illustrate the convergence of mucus currents with consequent concentration of the contained carcinogens of inhaled cigarette smoke, smog, radioactive "fallout," radioactive mine dust, etc. In the large bronchi, there is great concentration combined with slowing of the mucus raft, and here the epithelium is exposed to a maximum of carcinogenic action and bronchial carcinoma is most abundant. Concentration of carcinogens may be increased by dehydration as the raft of mucus moves over the conjoined bronchial area, in the direction indicated by the arrows, toward the hilus of the lung and ultimately the glottis. Although zones are marked off for the alveolated bronchioli (representing the alveoli), for the smooth-walled bronchioli, and the small, medium, and large bronchi, there is no attempt to represent these areas on a proportional basis. For instance, the outer alveolar zone would have to be immensely greater than it is to bring it into true relation to the area of the large bronchi. Most of the carcinogen-bearing smoke and smog falls on this great peripheral alveolar territory; its walls are not covered by true mucus but rather by alveolar mucoid fluid (Macklin[8, 9]), and no true cilia abound here so that transport of carcinogens seems to be largely intracellular and amoeboid in type. The dots indicate the carcinogens moving in the direction of the arrows. The broken transverse crescentic lines stand for the carinae of the large bronchi and trachea. This diagram is, of course, not intended as a universal indicator of the sites of bronchial cancer for not a few of these occur peripherally to the hilar region of the lung. As a watershed gathers in and drains away water so this "particleshed" gathers in and drains away carcinogens that have fallen upon it from the inspired air.

greatly thicken as it narrows, even to the extent of obstructing or blocking the tubes, particularly as it must gain volume from added secretions, and the explanation seems to be that it gives off water as it moves along (for alveolar air may lose water to alveolar fluid and be desaturated, Macklin[11]). Such a "boiling down" would further condense the carcinogens. Therefore, in the larger bronchi of the hilar region the carcinogens are tremendously concentrated. That is why the epithelial cells of the large bronchi, underneath this raft, are exposed more than are those of any other part of the bronchial tree to the delinquency-promoting action of carcinogens on cells. That is why most bronchial carcinoma develops in the hilar region. By the time the raft gets to the hilus, its diminution in area by convergence is as much as ten thousand into one.

SLOWING AT CONFLUENCES

Another factor making for heightened carcinogenic action in the hilar region arises from the fact that at the great bronchial confluences there is an inevitable lateral shift of much of the mucus current entailing a thickening of the mass at such points and delay in its onward progress. This makes these forkings the scene of extra accumulation and also a lingering of the carcinogen forces which then have leisure to act with great strength upon the underlying epithelium. This will be clear when we recall that the two streams of the inner walls of the bronchi which merge at a fork come to an end, so to speak, at the edge of their carina and can only proceed by turning out along the curving keel. Any illustration of the human trachea and large bronchi (von Hayek[15]) will show that the hilus of each lung is a confluence region with as many as four carinae. It is not difficult to see why the mucus currents here should slow down, for the ciliary burden must become much heavier rather suddenly from convergence of currents and deviations at carinae. Another point to be mentioned about the hilar region in this connection involves specially the bronchi to the upper lobes at the points where they enter the main bronchi and that is, that the mucus traveling down the medial side has to make a sudden turn as it climbs up the lateral wall of the main bronchus, and because of the upright posture it is moving against gravity. It is like walking on the ceiling. This site is said to be a favorite one for bronchial cancer, particularly on the right side. My readers are enjoined to consult a bronchial map (Boyden[2]) and try to figure out the course of masses of mucus proceeding along any of the branches centering in the hilus. When this visualization is done in three dimensions and attention is focused on the inside of the tubes, it will be realized that there is here (1) a rather sudden merging of currents of mucus entailing a thickening of the raft with an inevitable increase of the strain on the underlying cilia, which cannot possibly be reinforced in any way to meet it, and (2) a complex of devious courses of mucus streams as they curve out to avoid "falling over the edges" of the carinae and, thus, they undergo unavoidable accumulation and retardation in the process. If now they will see in this mucus coating of the large bronchi a hotbed of carcinogens, they will be educated to an understanding of the basic reason for

the hilus being par excellence the part of the entire field of the bronchial epithelium where carcinomatous change occurs. Why masses of mucus arriving at a carina come to the end of the road, so to speak, and are unable to go straight on, but must be deflected by special ciliary arrangement to one or other side is even more convincingly demonstrated by looking into the interior of a living bronchus through a bronchoscope; but a good substitute for this experience is had by viewing illustrations of bronchoscopic fields such as those of Fig. 125 of Brock.[3]

Then, too, it is more than possible that this long-acting concentrate of smoke products would functionally depress the oversmeared ciliary propellant making the current sluggish and the carcinomatous raft to lag, particularly in the hilar region. Ciliary paralysis, partial or complete, would thus constitute an accessory retarding influence. Metaplastic change even removes the cilia. All told, it seems very probable that in the hilar region of the bronchial tree there is more cancer-producing substance acting on the epithelium for a longer time than there is anywhere else in the air tract. The effective carcinogenous material is probably not intracellular; it is more likely that it is in the remains of phagocytes which carried it out of the alveoli and along the alveolar bronchioles (ducts) to the ciliated part of the air tract. Indeed, some of the material may never have been phagocytized at all but have been intercepted as particles by the sticky mucus of the raft. The carcinogen acts doubtless as a molecular solution upon the epithelium. Carcinogenic power probably varies directly with the concentration.

SMOGS AND RADIOACTIVE DUSTS

Inhaled cigarette smoke has been widely incriminated in bronchial cancer induction, but it is surely not the only offender, and the special vulnerability of the epithelium of the hilar bronchi to cancer must be related to all dusts and smogs containing carcinogens borne in the mucus currents passing over it. The mechanism would be the same for all. The outdrifting mucus raft affords the *only means* of eliminating particulate matter admitted to the lungs save that available for large masses when peristaltoid movements of the bronchial musculature (Macklin[7]) and coughing come into play. The air of great cities like Los Angeles is contaminated with the products of combustion of coal and oil and these, especially those of oil, are in very finely particulate form and attract water molecules to form smog. These minute smog particles are likely to travel right to the alveoli and impinge on the walls thereof. It is probable that smog always forms when very small particles are being carried along in the humid air of the bronchial tree. The danger of cancer induction is enormously increased if the particles are radioactive, as was the case in the dusty mines of Schneeberg and Joachimsthal (Lorenz[6]) where so many of the miners became victims of bronchial carcinoma. This breathing in of "hot" particles in certain unprotected industries is an invitation to lung cancer. Entire populations, in these days of the testing of thermonuclear weapons, may be subjected to this hazard, for the inhalation of relatively small quantities

of radioactive "fall-out" may ultimately result in a great crop of bronchial cancers. This could occur, of course, only in those people whose intake of "hot" dust was prolonged and insufficient at any one time to induce immediate serious illness. The conveyance of these radioactive particles in the mucus of the air tract and the concentration of the carcinogen in the hilar region would be like that described for inhaled cigarette smoke. It may take some thirty years or more of action of carcinogen concentrate from inhaled cigarette smoke to break down the contracancer defences in bronchial epithelial cells (Graham[4a]), but that from frequent exposure to radioactive fall-out would likely require less time. Chronicity is of the essence of carcinoma induction. Primary origin is doubtless in fields of epithelium, with progressive conversion of normal into cancerous cells, rather than in single cells or small foci of cells (Willis[16]), and there may be more than one such field (Ackerman[1]). The exact reason for the selection of any special field for cancerous change is not apparent. It may be a local hereditary predisposition. The same explanation may apply to those bronchial carcinomas which occur beyond the hilus; but here the exciting cause would be found, as for the others, in the chronic application of carcinogen concentrate. Slaughter and his associates have recently discussed field cancerization and multicentric origin.[13a]

TRACHEA

Why is the trachea less involved in cancer than are the large bronchi? Certainly it bears the end result of convergence of mucus currents and desiccation of the carcinogen-infiltrated mucus. Possibly it is because the mucus raft travels more rapidly in the straight trachea, and is not abruptly piled up and slowed as in the devious course of the hilar bronchi; and is not on the whole so adversely affected by gravitational influence as are certain parts of the large bronchi; and possibly because its cilia are not overburdened and are more efficient. Certainly there is not at the origin of the trachea as sudden and great an augmentation of the ciliary load as there is in the hilar region, as the cross section of the two main bronchial tributaries is not much different from that of the trachea. If one of the alternative explanations for the prevalence of hilar bronchial cancer be applied here, namely, that it is due to some sort of "heat stroke" by the entering column of hot smoke, the trachea should succumb before the bronchi and even this guess would apply only to smokers. If the cancer-producing action were primarily on the first part of the trachea more heavily involved than the great bronchi. By the time the mucus gets to the trachea it is doubtless depleted in carcinogens.

PREVENTION

For the cigarette smoker, the ideal course would be total abstinence from cigarettes; but short of this it is wise to exercise moderation and particularly to abstain from inhaling the smoke. With the dangerous smogs of cities, radioactive mine dusts, and "fall-out," elimination of the cause is the essential thing. Masks of proper type will aid in emergencies. Education of the public (Hudson[5]) will cut down the rate of incidence of bronchial cancer

which is already the most frequent carcinoma in the human male (Graham[4a]). Storm warnings are flying. Mayer[13] has affirmed that, at present acceleration, the death rate from lung cancer is expected in the next quarter of a century to exceed that from *all other cancers combined.*

SUMMARY

The smoker who inhales brings by far the most extensive area of his lungs, the alveolar, into play to catch carcinogens. These smoke particles, deposited on the inner surface of alveoli and air tract, are returned to the pharynx in a layer of moving mucus which converges and lingers in the hilar region. Here the carcinogens are specially concentrated and stagnated, and they act with high intensity and chronicity on the epithelium of the great bronchi, to induce more cancer than elsewhere in the bronchial tree. Other carcinogenic particles, in smogs and radioactive dusts, have a similar mode of application to the bronchial epithelium with disastrous result.

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PHYSIOLOGIC ASPECTS OF BRONCHOGENIC CARCINOMA

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AT the present time, the treatment of choice for bronchogenic carcinoma is extensive surgery, the only approach which offers the possibility of cure. Primarily, as a consequence of the problems posed by bronchogenic carcinoma, the technical aspects of thoracic surgery have been intensively studied during the past two decades. Surgical techniques, as well as operative and postoperative procedures, have been developed to the point that pneumonectomies are common operations in all our large hospitals. Many of the successful operations in the past, however, have resulted in complete respiratory crippling of the patient. Thus, the physiologic problem of over-all pulmonary function and pulmonary reserve has become of critical importance. In fact, lack of adequate pulmonary reserve is probably the only major contraindication to pneumonectomy at present, outside of the extension and metastasis of the tumor itself.

This situation has been a great stimulus to the study of pulmonary function. As a result, methods have been developed to determine pulmonary reserve, and even to estimate with some accuracy what the respiratory status of a patient will be after surgery. These procedures are not limited to use in large university research laboratories; many of them are sufficiently simple and inexpensive to be utilized in any hospital that has facilities for surgical exploration of the chest. Such testing, of course, is time consuming and some training of the examiner is necessary. It often provides clinically valid answers to the questions important to surgical evaluation, and the value in prognosis warrants the time and effort required.

COMMON PULMONARY FUNCTION TESTS

The requirements of physiologic testing vary considerably from patient to patient. Sometimes a few simple studies will provide clear and unequivocal information, while a more thorough evaluation is needed for some patients. The purpose of the following description is to define the basic minimum study necessary to prognosis in the easier cases; such a study will also serve as groundwork for more detailed evaluation in the difficult cases.

Basic Ventilatory Tests.—Simple ventilatory tests should be done at the time of diagnosis.[1] Maximum breathing capacity has been so well standardized

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that it is a useful point of reference, even though in certain respects it may be considered somewhat unphysiologic. Some form of resting, exercise and recovery ventilatory test provides valuable information. These tests can be correlated to give various ventilatory coefficients. Spirographic tracings are informative, since they show over-all compliance and volume changes, both qualitative and quantitative. These tests require simple instruments and only a minimum of training on the part of the operator. Tests, such as breath holding, pneumatometry, and others, are used by some workers to amplify results further.

Radiologic Techniques.—The usefulness of fluoroscopic study of the heart silhouette is generally recognized. Such studies are usually amplified by electrocardiograms and determinations of hematocrit, venous pressure and circulation time. These evaluations are particularly important when a pneumonectomy is contemplated, since right-sided heart failure may ensue in patients with emphysema in the remaining lung and any significant degree of pulmonary hypertension.

Fluoroscopy is also useful in detecting specific abnormalities affecting pulmonary function, such as a weak diaphragm. Inspiration-expiration postero-anterior x-rays of the chest should be correlated with vital capacity tests. While measurement of lung areas, as shown in x-rays, with a planimeter does not take into account the effect of pathologic lung changes, it does give a rough basis for differentiating the ventilation volume of each lung and for estimating residual volume.[2]

Radiologic information can be supplemented by simultaneous intrapleural pressure readings, using standard pneumothorax equipment, during quiet and maximal respiration. These data are particularly useful in determining pulmonary compliance on both sides.

Intrapulmonary Gas Mixing Tests.—The study of residual air and intrapulmonary gas mixing has become a common procedure in many hospitals. Either the closed-circuit helium or the open-circuit nitrogen method will provide information as to the presence of overdistention and the mixing of inspired air with alveolar gas. While these tests permit a more accurate definition of these aspects of pathophysiology than do radiologic methods, they do not differentiate between the two lungs, and hence are, we feel, more applicable to the analysis of a diffuse disease process than to the localized process of a cancer. They may, however, contribute to prognosis after differentiation has been established by other techniques.

Bronchospirometry.—Although bronchospirometry is the best single differentiating function test now available, the discomfort it causes the patient and the long testing period have limited its use. Also some training is required for correct evaluation of bronchospirometric findings with the problems of catheter blockage and the effects of the catheter itself upon the air flow. Since it is the most accurate technique we have for determining volume ventilation, oxygen consumption, and intrapulmonary mixing for each lung separately, the value of bronchospirometry outweighs these difficulties in practically every instance in which the results of simpler tests are ambiguous. It is especially valuable in

assessing the condition of a single lobe in cases where a choice must be made between a lobectomy or a pneumonectomy involving the sacrifice of normal tissue. Studies should always be made during exercise (with foot pedals) as well as at rest.[3]

It must be remembered that bronchospirometry can evaluate the function of a lung or a lobe only under the conditions prevailing at the time of the examination. Predictions of postoperative course are often found to be conservative because they do not take into account the great adaptiveness of the organism to the postoperative situation.

Blood Studies.—Many of the simpler studies involving arterial oxygen saturation can be done with a photoelectric ear oximeter. The clinical estimate of oxygen in the blood, however, requires experience. Isolated arterial oxygen values, of course, are of little significance, but desaturation on exercise is important to know, particularly when it can be correlated with oxygen consumption.[4] The breathing of pure oxygen may demonstrate abnormalities of gas distribution and blood perfusion.[5]

The detection of respiratory acidosis, as reflected by arterial CO_2 tension, is important during all stages of operative treatment—preoperatively, during the operation, and particularly in the immediate postoperative period. In most laboratories this value can be readily ascertained by determining the arterial blood pH and the direct plasma CO_2 content, calculating the tension by the Henderson-Hesselbalch equation. The Van Slyke apparatus is found everywhere, pH meters are coming into widespread use, and the range of their serviceability fully justifies their purchase. Arterial puncture is a simple procedure that should involve no hazard.

Simultaneous blood-gas studies, with calculation of venous admixture, diffusion gradients, and so forth,[6] are beyond the scope of most hospital laboratories. Such studies are not always as informative in determining pulmonary function in cases of bronchogenic carcinoma as in cases of diffuse disease.

Admittedly, lung function tests are not as well standardized as routine clinical use makes desirable, and often the clinician must work with improvised equipment. However, the information gained, even with the most limited materials, can aid in determining the type of surgical procedure to be undertaken and even, in some cases, whether an operation is feasible. They also are a useful guide to prognosis of postoperative lung function, and can alert the surgeon to operative and postoperative hazards.

THE EVALUATION OF PRE-EXISTING PULMONARY ABNORMALITIES

Pre-existing pulmonary abnormality is very common in patients in the age group in which bronchogenic carcinoma is most frequent. Some degree of emphysema is almost the rule; in addition, such disorders as fibrosis and pleural thickening are often encountered. These abnormalities introduce special diagnostic problems because of the difficulty of isolating the effects of the tumor from the general pulmonary insufficiency.

In some cases, a pre-existing abnormality is easily recognized. Obstructive emphysema (not due to the tumor) is manifested by the typical delay in expiration as shown on the spirogram, as well as by the increase of residual air in relation to vital capacity. Trapping of the "normal" lung by pleural fibrosis is also easy to detect but, in many instances, it is difficult to decide whether there is any pulmonary insufficiency in addition to that directly due to the tumor. It is dangerous to assume that the nonaffected side is normal, especially when radiologic or clinical evidence suggests abnormality. If spirographic tracings do not give volume and velocity measurements which are at least one half of the predicted value, some degree of ventilatory difficulty on the normal side should be presumed. Also, abnormal intrapleural pressures on the contralateral side confirm the presence of a generalized pathologic condition in addition to the tumor.

Even when abnormality of the other lung has been established, the degree of respiratory embarrassment due to that lung may be difficult to determine. Occasionally this problem can be approached by trying to approximate the degree of embarrassment due to the tumor and its secondary manifestations, and subtracting this from the total respiratory deficiency. More often, conditions secondary to the tumor will be impossible to estimate; even where there is clear evidence of emphysema, it may be difficult to tell whether it is compensatory or independent of the tumor, or whether it is reversible or not. A study of the area change in posteroanterior x-ray films made during inspiration and expiration may give a reasonable basis for determining the volume ventilation of the contralateral lung; however, in many cases, bronchospirometry will be very nearly mandatory. Every effort should be made to determine the efficiency of the other lung, even if it involves referring the patient to a better-equipped institution; otherwise there is the risk that successful surgery may actually shorten the patient's life.

A good many investigators have attempted to develop more accurate methods of evaluation. For example, angiocardiography has been used to demonstrate not only blood flow through atelectatic tissue, but also through anastomotic channels in the tumor mass.[7] Cardiac catheterization, using a balloon-tipped catheter, has been applied in determining the effects of blocking pulmonary artery blood flow to an affected lobe. There have been attempts to forecast partially the effects of possible pneumonectomy by blocking simultaneously both blood and air flow to the lung to be removed.[8] Although these procedures may hold out hope for the future, they are too complicated and too hazardous for clinical application at the present time.

It should be pointed out that in a good many instances the elementary methods of determining respiratory function efficiency will suffice to clear up doubts about the feasibility of an operation. This is particularly true in those cases in which severe exertional dyspnea seems out of proportion to the amount of damage indicated by lung function testing or visible radiologically. In many cases of lung cancer, the subjective feelings of dyspnea bear almost no relation to the real extent of abnormality. This is probably a result of increased

stretch reflex irritability in an area of "stiffened lung" due to infiltration. In such cases, other lung function tests will show virtually normal values.

PULMONARY FUNCTION TESTS DURING THERAPY

Surgical procedures which involve only the resection of damaged tissue are likely to result in improved lung function by improving the distribution of blood and gas in the lungs as a whole. In such cases pulmonary function is rarely a problem after the operative and postoperative phases. However, in some instances where preoperative studies have revealed only a well-localized peripheral tumor, evidence of spread at thoracotomy may call for pneumonectomy. This will sacrifice a good deal of lung tissue, reduce ventilation, and shunt the whole of the cardiac output through the remaining lung. If there is already gross obstructive emphysema with respiratory acidosis, the patient may be unable to ventilate sufficiently after the operation. If there is pulmonary hypertension with early signs of right ventricular strain, the pneumonectomy may be enough to precipitate right heart failure.

If pulmonary reserve is adequate and an operation is undertaken, the patient's respiration must be watched carefully during the operation and particularly postoperatively. Ventilation during the operation is usually not a problem, since it is controlled by the anesthetists with a direct view of the thorax, although even in this situation respiratory acidosis may occur unless special attention is paid to tidal volume. In some of the better-equipped hospitals the end-expiratory CO_2 content is continuously followed by automatic analyzers, so that the smallest degree of acidosis can be detected and checked.[9] In institutions without this equipment, a periodic check of arterial CO_2 tension can be made by analysis of CO_2 content and pH values.

After the thorax is closed, but before the patient completely recovers consciousness, respiration is liable to become too shallow to maintain adequate tidal volume. In the past there has been a tendency to administer oxygen to such patients, which treats the hypoxia selectively and masks impending respiratory acidosis. It is our conviction that the intermittent positive pressure apparatus is preferable in respiratory failures of this kind, since it restores adequate ventilation, thereby preventing the accumulation of CO_2 as well as ensuring normal oxygen content in the alveoli.

A number of other postoperative developments such as pleural effusions, atelectasis, paradoxical respiration, and pericardial tamponade may tend to diminish respiratory efficiency. In our experience, painful respiration, usually at the site of incision, has been the most frequent cause of respiratory embarrassment. It can usually be controlled by a paravertebral alcohol block or Novocain infiltration of the incision.

In the later postoperative phases, scoliosis is perhaps the greatest danger, especially after pneumonectomy with thorocoplasty. The occurrence of scoliosis, which may mean the difference between respiratory crippling and a reasonably normal life, can be prevented only by diligent physical therapy. It has been our practice to institute such therapy before surgery and continue it for about six weeks, until the patient is able to carry on the exercises by himself.

Last, it should be pointed out that palliative radiotherapy should not be contemplated in patients with any degree of respiratory embarrassment unless pulmonary function tests are performed. It must be remembered that such therapy results in immediate local swelling and edema which may be followed by fibrosis involving a good deal of normal tissue. The end product is devascularization, focal emphysema, and loss of alveoli, with a consequent reduction in the pulmonary capillary bed and a diminished alveolar surface area. If there is any considerable pulmonary insufficiency to begin with, radiotherapy can easily result in making a patient a respiratory cripple.

SUMMARY

The surgical therapy of bronchogenic carcinoma demands preoperative study of pulmonary function. In many cases simple ventilation studies and inspiratory-expiratory posteroanterior x-rays are sufficient. In difficult cases where further study is required, differential bronchospirometry is the most valuable procedure. The isolation of the effects of the tumor from pre-existing and consequent abnormalities may be very difficult.

Inadequate ventilation during surgery and in the early postoperative phase may readily occur. Pain in the chest may restrict ventilation. These factors should be watched for. Scoliosis may develop later and be of sufficient degree to restrict ventilation. Radiotherapy may markedly interfere with pulmonary function.

Detection, prevention, and energetic therapy of causes of pulmonary insufficiency are mandatory for best results in the surgical treatment of bronchogenic carcinoma.

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